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INTRACAPSULAR CATARACT EXTRACTION

STATISTICAL SURVEY OF FIVE HUNDRED CONSECUTIVE CASES

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In this report is submitted a statistical analysis of the records of 500 consecutive cases of intracapsular extraction performed by me and my associates on the staff of the University of Wisconsin General Hospital up to December 1940. I reported 200 of these cases before the American Academy of Ophthalmology and Otolaryngology in 1937.[1] The data concerning these two series of intracapsular operations, 200 in the first and 300 in the second, have been combined here in order to present a more comprehensive survey of our results.

A full discussion of the operative technic employed, namely, the forceps expression method, together with the preoperative and postoperative care of the patient, was given in the previous paper and will not be repeated here. This report, therefore, will be limited in this respect to such additional information as has been gleaned from experience in the second series of 300 cases. Since these data were first compiled, my colleagues and I have performed about 400 additional intracapsular extractions, but a detailed analysis of the case reports of this series has not yet been made. At the outset, I may state that we have retained the same technic as that originally described, with only minor variations.

Experience in a series of operations now approaching 1,000 has served to reenforce our conviction of the soundness of the intracapsular method of cataract extraction, and in my opinion it should be the operation of choice in most cases of senile cataract.

STATISTICAL ANALYSIS OF FIVE HUNDRED CASES OF INTRACAPSULAR EXTRACTION

The ages of the patients are shown in table 1, in which the cases are grouped according to age decades, from 30 to 90 years. The youngest patient to be operated on was 33 and the oldest 87 years of age.

The state of maturity of the cataracts is shown in table 2, 272 being classified as mature, 173 as immature and 55 as hypermature.

ETIOLOGIC FACTORS AND ASSOCIATED DISEASES

The primary cause of the cataract could not be determined in most instances. Diabetes was present, in various stages, in 39 cases; in 17 of these cases diabetic retinitis was a complication. The diabetes appeared to be the primary cause of the cataract in only a limited number of cases.

In 7 cases there was high myopia. In such cases operation is usually performed by the extracapsular method, but because of the immaturity

TABLE 1.—*Ages of Five Hundred Patients Subjected to Intracapsular Cataract Extraction*

Age, Years	No. of Cases
30 to 40	2
40 to 50	27
50 to 60	79
60 to 70	166
70 to 80	194
80 to 90	32
	500
Sex	
Males	275
Females	225
	500

TABLE 2.—*Description of Cataracts*

Type of Cataract	No. of Cases
Mature	
Sclerosed	80
Ordinary senile (cortical)	192
	272
Immature	
Amber nucleus, clear cortex	115
Ordinary cortical, including postsubcapsular and intumescent	58
	173
Hypermature	
Shrunken	20
Fluid cortex; rubbery capsule	26
Soft cortex	2
Sclerosed	7
	55
Grand total	500

Read at a meeting of the Chicago Ophthalmological Society, May 19, 1941.

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1. Davis, F. A.: Personal Experiences with Intracapsular Cataract Extractions, Tr. Am. Acad. Ophth. **42**:218, 1937; Arch. Ophth. **19**:867 (June) 1938.

of the cataract the intracapsular procedure was employed. There was no loss of vitreous in any of these cases.

Chronic simple glaucoma was present in 12 cases. In 3 cases a previous trephining or a modified Lagrange procedure, with inclusion of the iris, was done. A small bead of vitreous was lost in 1 of these cases, that of a patient aged 81, when the iris pillar was replaced. No vitreous was lost in the other 11 cases. In all cases the glaucoma had been brought under control by treatment, no patient having high intraocular tension at the time of operation. In 2 cases the tension was very low, with deep glaucomatous cupping. The designation of the condition as glaucoma in these 2 cases of course is questionable.

In 2 cases cataract of allergic origin was associated with severe and extensive dermatitis venenata, of long standing. One patient had had a detachment of the retina for eight years or longer. In a number of cases there was subluxation of the lens, the condition being congenital in some cases and the lens being hypermature and shrunken in others, with vitreous in the anterior chamber. Other, rarer, types which were encountered and the associated lesions are shown in table 9.

TABLE 3.—*Method of Operation*

	No. of Cases
Preliminary iridectomy	223
Extraction combined with iridectomy	246
Simple extraction	
Without iridectomy	3
Peripheral iridectomy	28
Total	500

In table 3 are recorded the methods of operation employed. Iridectomy of some type was performed in practically every case in this series.

I personally prefer, and generally use, extraction combined with complete or peripheral iridectomy. Simple extraction, when uncomplicated by incarceration or prolapse, produces the ideal postoperative result, but, as I have previously pointed out, from the standpoint of safety and ease of extraction complete iridectomy has a distinct advantage. With some of the younger subjects, with healthy, active irises, for whom a perfect cosmetic result is desirable, we employ simple extraction with peripheral buttonhole iridectomy. However, it cannot be denied that extraction undeniably is more difficult through the round pupil, especially when, as is not infrequently the case, the pupil cannot be dilated sufficiently to permit easy passage of the lens.

In most of the 31 cases in which the lens was extracted through the round pupil, the subjects were young. In all cases the method was successful from an operative and a visual standpoint, but postoperative prolapse of the iris beneath the conjunctival flap, requiring excision, developed in 3 cases. This complication is serious and, in my opinion, should be avoided at all costs. It is especially important that it be avoided in older, feeble and uncooperative subjects.

In table 4 is recorded the condition of the capsule on delivery of the lens. In 424 (84.8 per cent) of the cases the capsule was intact (+), and in 76 (15.2 per cent) it was broken (±).

TABLE 4.—*Condition of Capsule on Delivery of Lens*

	No. of Cases	Percentage
Capsule intact (+)	424	84.8
Lens and capsule (capsule was ruptured during or after passage through wound but was completely removed (±)	76	15.2
Total	500	

At times a portion of the capsule of the lens may become caught in the wound if it ruptures during delivery. The incarcerated portion can frequently be pulled out by reintroduction of the smooth forceps just inside the lips of the wound. In the cases in which we failed to deliver the lens with the capsule the operation was classified as "attempted intracapsular extraction." These cases are not included in this survey, since extracapsular extractions were done. They numbered 105, or 17.4 per cent, of a total of 605 operations. Thus, intracapsular delivery was successful in 82.6 per cent of the entire series in which it was attempted.

TABLE 5.—*Tabulation of Successful and Unsuccessful Intracapsular Deliveries*

		Number	Percentage
Total number of intracapsular operations attempted		605	
Delivery in capsule	500		82.6
Extracapsular delivery	105		17.4
First series: operations attempted		252	
Delivery in capsule	200		79
Extracapsular delivery	52		21
Second series: operations attempted		353	
Delivery in capsule	300		85
Extracapsular delivery	53		15

In table 5 the successful and unsuccessful deliveries are shown separately, as well as combined. It will be noted that in the first series 200, or 79 per cent, of the cataracts were delivered in capsule, while in the second series 300, or 85 per cent, were delivered in capsule.

Our experience with rupture of the capsule is similar to that previously reported. It is most common with the intumescent, slightly swollen lens with a tense capsule. In our first series

we had more failures with the large, hard, brown, sclerosed type of lens in which no soft cortex was present. Such a lens will not mold, since it consists of a hard nucleus only. In the second series we have been somewhat more successful with this type, since we avoid taking too large a bite or grasp of the capsule and thereby prevent its rupture. More emphasis is placed on exertion of pressure with the spoon, and thereby we have had fewer ruptures of the capsule in extracting this type of cataract. The capsule may be noted to be torn between the jaws of the forceps after the lens has been delivered; but if one avoids releasing or regrasping the capsule, successful intracapsular delivery can frequently be accomplished in spite of this.

The hypermature lens with fluid cortex and distended, taut, rubbery capsule still presents a problem for removal by the intracapsular method, since it is impossible to grasp the capsule. There were 26 cases of this type, as will be noted in table 2. In 11 of these cases we removed the cataract successfully by the Smith method, with external pressure alone, without benefit of forceps. Vitreous was lost in but 1 of these cases, and then only a drop, with final vision of 20/20. Application of external pressure alone is also at times successful in delivery of the intumescent lens if the age of the patient is sufficiently advanced, and it should be attempted if the capsule cannot be easily grasped.

The immature lens, with a central nuclear haze, clear periphery and soft, pultaceous, clear cortex, is the ideal type for intracapsular extraction. The capsule moves freely on the underlying cortex. It is thus easily grasped without rupture, and delivery in the intact capsule is successful in almost 100 per cent of cases.

As was noted in my previous communication, the operation is most successful in persons of the age group from 60 to 90 years, since the zonule appears weakened and breaks easily. However, my associates and I have grown much less apprehensive concerning delivery in capsule in persons of the younger age group, from 40 to 50. As was previously pointed out, the soft, white, rapidly developing cataract in younger subjects has frequently proved surprisingly easy to deliver. This second series, of 300 operations, has confirmed my previous experience in this regard. Intracapsular extraction in young subjects, under 40 years of age, is usually not successful, especially when the cataract is immature and partly clear or is of the congenital or juvenile type, since the zonule is tough and elastic and will not rupture easily. Cataracts of allergic origin and those which develop from dinitrophenol poisoning cannot usually be delivered in capsule in subjects under 50 years of age.

In any case, if the zonule does not break readily with moderate pressure on the globe, we usually abandon the effort and remove the capsule with the Fuchs capsule forceps.

PROLAPSE OF THE VITREOUS

In table 6 are indicated the cases in which vitreous was lost in any amount whatever, the amount recorded in the description of the operation, the time of the loss and the final vision obtained. I make a practice of recording "vitreous lost" in any case in which the hyaloid membrane ruptures, as evidenced by sudden deepening of the chamber, and in any case in which the slightest film of vitreous is noted on the spatula, even though no measurable quantity is lost. As will be noted, there was loss of vitreous in 36 cases, or 7.2 per cent of the 500 cases of intracapsular extraction. The 10 cases in which vision was less than 20/30 will be discussed more fully later. The incidence of loss of vitreous was only 6 per cent in the first series, of 200 cases. The increase in the second series is probably due to the fact that the selection is now less careful than in the first series and, also, that all members of the staff, including house officers, are now using the intracapsular method.

Our incidence of loss of vitreous was lower after intracapsular extraction than after extracapsular extraction, at least in a small series of 100 cases of the latter operation performed during the period of our first series of 200 intracapsular operations, in 9 per cent of which there was loss of vitreous. Gradle,[2] Gailey[3] and others have

TABLE 6.—*Summary of Data in Cases in Which Vitreous Was Lost* *

Operative Record of Amount Lost	No. of Cases
Tiny bead to 1 drop	16
Two to 3 drops	7
Four drops	4
Moderate loss	5
Eight drops	1
Vitreous flowed out (liquid)	3
	36
Fluid vitreous noted in 7 cases	

Time of Loss of Vitreous	No. of Cases
After section	7
During delivery	4
After delivery of lens	19
On replacement of pillar	6
	36

Vision	No. of Cases
20/15	4
20/20	12
20/30	9
20/40	2
20/50	1
20/70	1
20/100	1
20/200	4
Light perception	1
Unknown	1
	36

* The total of 36 cases represents 7.2 per cent of the 500 cases in which this operation was performed. The capsule was intact in 34 cases and broken in 2 cases.

2. Gradle, H. G.: Intracapsular Versus Extracapsular Extraction of Cataract, Tr. Sect. Ophth., A. M. A., 1933, p. 186.

3. Gailey, W. W.: A Report on Two Hundred Cataract Operations, Illinois M. J. **72**:528 (Dec.) 1937.

reported similar experiences, while Berens and Bogart,[4] in a recent review of 1,004 operations, reported that the incidence of loss of vitreous was about the same with the two methods, namely, 9.9 per cent for the intracapsular and 9 per cent for the extracapsular procedure. Knapp,[5] in his series of 500 cases, reported loss of vitreous in 8.4 per cent; Greenwood and Grossman,[6] in a series at the Massachusetts Eye and Ear Infirmary, in 6.2 per cent, and Bothman,[7] in a series in India, in 4.5 per cent.

In table 7 are recorded the data in the 11 cases in which there was loss of vitreous and vision was less than 20/30. In all but 4 of these cases the lowered visual acuity appeared to be due to previous disease, such as diabetic retinopathy (cases 5 and 6), old chorioretinitis (case 8), macular hemorrhage due to hypertensive retinopathy (case 3), chronic simple glaucoma (case 1), amblyopia ex anopsia associated with a subluxated lens of fifteen years' duration (case 9) and iritis of long standing with synechiae (case 10). In case 2 a drop of vitreous was lost. The healing was prompt, the patient being discharged on the fourteenth postoperative day. This patient did not return for final refraction.

TABLE 7.—*Analysis of Cases with Loss of Vitreous and Vision of Less than 20/30*

Case No.	Description	Vision	Capsule
1	Bead on replacement of pillar (C. S. G.*)	20/40	Broken
2	One drop after delivery (vision on 14th day)	20/40	Intact
3	Three drops after delivery (hypertensive retinopathy; macular hemorrhage)	20/50	Intact
4	Three drops (fluid vitreous)	20/70	Intact
5	One drop after delivery (diabetic circinate retinopathy, both eyes; macular lesions)	20/100	Intact
6	One drop after delivery (diabetic retinopathy; macular lesions in both eyes)	20/200	Intact
7	Four drops (vision 20/30 on discharge); late iritis, with reduction of vision to	20/200	Intact
8	Moderate loss (fluid; complicated cataract; old central chorioretinitis; absolute glaucoma in other eye)	20/200	Intact
9	Tiniest amount (subluxated lens 15 years; lens lifted out with forceps; amblyopia ex anopsia)	20/200	Intact
10	Light perception; complicated cataract synechiae; secondary glaucoma in both eyes	Light	Intact
11	Four drops with section	Unknown	Intact

* C. S. G. indicates chronic simple glaucoma.

Credit for the notable reduction in the incidence of loss of vitreous in cases of intracapsular extraction undoubtedly belongs to Van Lint, who introduced the use of akinesia. Certainly, the amount of vitreous lost has been materially lessened by the elimination of the possibility of the patient's squeezing the eye. Solution of tribromoethanol U. S. P. was used in 10 per cent of this series of operations. We still use it in operations on highly nervous, unruly or ignorant subjects, especially when the eye is extremely prominent or the tension elevated. With added experience we have had no occasion to change the conclusions which I expressed in a communication on this subject several years ago.[8] My colleagues and I are now using pentothal sodium in selected cases, but our series is not sufficiently large to justify a report on the results at this time.

In table 8 are recorded the cases of incarceration and prolapse of the iris. Prolapse occurred in 7 cases, in 3 after simple extractions; in 2 of these cases the complication was apparently brought on or aggravated by postoperative vomiting. Excision of the prolapsed iris was usually made as soon as it was discovered. Case 6 is of interest because of the profound coma which developed on the operating table, the coma apparently being due to an idiosyncrasy or an unusual response to pentobarbital sodium, which was given prior to operation. A dose of 1½ grains (0.097 Gm.) was administered by mouth fifteen minutes prior to operation. The patient remained irrational throughout the night and was uncontrollable. Prolapse of the iris under the flap, and probably loss of vitreous, may have occurred, although the conjunctival flap was not disturbed and the sutures were in place. In case 7 severe hyphemia with prolapse followed a blow on the eye. In case 8 there was a simple incarceration of one pillar, with no visible prolapse. Healing was

TABLE 8.—*Incarceration and Prolapse of the Iris*

Case No.		Visual Acuity
1	Prolapse, second day; simple extraction; vomiting	20/20
2	Prolapse, second day; simple extraction; vomiting	20/20
3	Prolapse, second day; simple extraction; hyphemia	20/30
4	Prolapse, eleventh day; one pillar; overactivity at home	20/20
5	Prolapse, one pillar; patient struck eye	20/40
6	Prolapse, one pillar; patient comatose on table; irrational; "hammock pupil"	20/50
7	Prolapse, one pillar; patient struck eye; wound sprung; hyphemia	H. M.*
8	Incarcerated pillar; secondary glaucoma	H. M.
	Adherent pillar, with no prolapse or complications, 21 cases	

* H. M. indicates hand movements.

4. Berens, C., and Bogart, D.: Certain Post-Operative Complications of Cataract Operations, Tr. Sect. Ophth., A. M. A., 1938, p. 238.

5. Knapp, A.: The Complications of the Forceps Intracapsular Cataract Operation Based on an Analysis of 500 Successive Cases, Tr. Am. Ophth. Soc. **34**:162, 1936.

6. Greenwood, A., and Grossman, H. P.: An Analysis of 1,343 Intracapsular Cataract Extractions by Forty-Eight Operators Following the Verhoeff Method, Tr. Am. Ophth. Soc. **33**:353, 1935.

7. Bothman, L.: Complications of Cataract Surgery in India, Illinois M. J. **62**:243, 1932.

8. Davis, F. A.: Tribromethanol (Tribromethyl-Alcohol, Avertin) as an Anesthetic in Eye Surgery, Tr. Am. Ophth. Soc. **29**:47, 1931.

prompt, with good vision, but secondary glaucoma developed, with pain and gradual deterioration of vision to perception of hand movements. Repeated operation failed to relieve the condition, and the eye was finally enucleated.

The records show an additional 21 cases in which one pillar was adherent to the line of incision. These cases presented no symptoms; the eyes healed promptly, and the visual acuity was not affected up to the time the records were reviewed. I always regard such cases with some concern, since an adherent pillar may be followed by a secondary rise in intraocular tension, as in case 8, previously cited. On the other hand, I have seen and followed for years many patients with this condition who showed no evidence of any complication.

HEMORRHAGE INTO THE ANTERIOR CHAMBER

Postoperative hemorrhage into the anterior chamber was noted in 46 cases (9.2 per cent), the time of occurrence ranging from the second to the seventeenth day. All of these hemorrhages, except in 5 instances, occurred from the second to the sixth postoperative day, and the great majority of them were on the fourth, fifth or sixth day. All were confined to the anterior chamber except in 3 cases, in which the vitreous was also invaded. In 12 cases they were due to trauma, but in a much larger number, 31 cases, hemorrhage seemed to occur spontaneously, without injury of any kind. In many cases the hemorrhages were small and cleared up promptly, but in a number the amount was considerable, the blood completely filling the anterior chamber and, in 3 cases, causing bulging of the flap, with external oozing. In a few cases bleeding was recurrent.

In my first series, of 200 cases, postoperative hyphemia occurred in 7 per cent; in the next 100 cases, in 9 per cent; in the fourth 100 cases, in 5 per cent, and in my most recent series, the fifth 100 cases, in 18 per cent. My average for the entire series, namely, 9.2 per cent, aproximates closely that given by other investigators (Wright,[9] 10 per cent; Vail,[10] 8 per cent, and Knapp,[11] in series of 100 cases reported in 1935, 9 per cent). However, Berens and Bogart[4] recorded only 4 per cent, while Bothman,[7] in an Indian series, reported 3.6 per cent.

In table 9 are summarized the data in all the instances of postoperative hemorrhage observed in the 500 cases, with notations as to the day on which the bleeding was first observed and the final visual acuity obtained.

As will be noted, in all but 8 of the 46 cases of postoperative bleeding final vision was 20/30 or better. In only 5 cases was the final visual acuity 20/70 or less. In 2 of these cases the patients were diabetic, vision in 1 instance being 20/200; the poor acuity in this case was entirely due to diabetic retinopathy, the blood being slight in amount and quickly absorbed. The patient whose final vision was limited to perception of hand movements struck the eye; the wound sprang; the iris prolapsed, and there was bleeding into both the vitreous and the anterior chamber. The patient whose vision was 20/100 was uncontrollable, twice pulling off the bandages, and on the eleventh day had a hemorrhage into the vitreous and the anterior chamber.

TABLE 9.—*Data on Cases of Postoperative Hemorrhage into Anterior Chamber* *

Onset Day	No. of Cases	Vision	No. of Cases	Cause	No. of Cases
2d.....	3	20/15.....	13	Unknown.....	31
3d.....	3	20/20.....	14	Trauma.....	12
4th.....	8	20/30.....	8	Vomiting with prolapse of iris.....	1
5th.....	10	20/40.....	2	Prolapse of iris.....	1
6th.....	16	20/50.....	1	Polycythemia vera	1
7th.....	1	20/70.....	2		46
8th.....	1	20/100.....	1		
9th.....	1	20/200.....	1	Anterior chamber..	43
10th.....	1	Hand movements.....	1	Anterior chamber and vitreous.....	3
11th.....	1		46		46
17th.....	1				
Unknown..	1				
	46				

* The total of 46 cases represents 9.2 per cent of the 500 cases in which intracapsular extraction was performed.

My study so far reveals no definite cause for the bleeding aside from postoperative trauma. Routine studies of the blood, including determination of coagulation and bleeding times, were made on practically all the patients. Special studies, including a platelet count, the tourniquet test and determinations of the vitamin C, prothrombin and calcium contents of the blood, were made on a large number of the patients, the results of which are to be reported later by my associate, Dr. E. E. Neff. A poor section, too far in the sclera, appears to predispose to postoperative hemorrhage. Two cases of hemorrhage were observed after simple extraction. In both these cases prolapse of the iris was caused by vomiting on the night of operation. Hyphemia is rare after a purely corneal section, as revealed by the Bothman series of 1,000 operations in India. Vail concluded that the bleeding is "the result of wound reopening and the rupture of newly formed corneo-episcleral blood vessels at

9. Wright, R. E.: Lectures on Cataract: Posterior-Segment Complications in Post-Operative Period; Some Difficult Extractions, Am. J. Ophth. **20**:376 (April) 1937.

10. Vail, D. T., Jr.: On Hyphema After Cataract Extraction, Tr. Am. Ophth. Soc. **31**:496, 1933.

11. Knapp, A.: Intracapsular Operation for Cataract: Report on Fifth Hundred Successive Extractions, Arch. Ophth. **13**:823 (May) 1935.

the section, and rarely from rupture or diapedesis from diseased iris vessels of inflammatory origin." He suggested the interesting theory, first advanced by von Grosz, that "increase of intraocular pressure and over-filling of the anterior chamber constitutes a 'crucial moment' when even the slightest lid pressure or ocular movement would be sufficient increment to cause the wound to reopen."

I am inclined to agree with this theory, since the time of bleeding in most cases is after the first dressing, when the wound is usually closed. Furthermore, on a few occasions bleeding has occurred at the exact moment of the first dressing. Therefore, in my opinion, the needless dressing of the eyes should be avoided and the first dressing postponed until the fourth day. Obviously, extreme care in all postoperative dressings is of the utmost importance, and undue pressure or manipulation of the lids should be avoided. Loss of vitreous does not appear to predispose to postoperative bleeding; in fact, the reverse seems to be true.

Postoperative bleeding is a most annoying complication, which, fortunately, rarely seriously affects the final result. The corneoscleral section, with the conjunctival flap, unquestionably predisposes to hemorrhage, since statistics reveal that bleeding is less common after a pure corneal section. However, I believe that most surgeons of the present day would be loath to give up the conjunctival flap and conjunctival sutures. Perhaps the deep corneoscleral suture, as advocated by Kalt,[12] Liegard,[13] Stallard,[14] Verhoeff,[15] McLean[16] and others, may prove to be the answer to the problem. I have used most of the various types of deep sutures but am not yet satisfied with any of them. Corneoscleral suturing is difficult and certainly complicates the operation. Sutures of the Kalt or the Stallard-Liegard type do not appeal to me, since they traumatize the cornea unduly and, further, fail accurately to approximate the edges of the wound. McLean's and Verhoeff's sutures produce a satisfactory closure, but their use is difficult in my hands. At present I place patches over both eyes for seven days, and so far this appears to have greatly reduced the number of cases of hyphemia. I believe that vigorous movements and squeezing of the fellow eye after removal of the patch may contribute to partial springing of the wound beneath the conjunctival flap of the eye operated on, with rupture of newly formed blood vessels. Suture of the deep wound might possibly avoid this, if the suturing was accurate and adequate.[17] However, I should be loath to abandon the conjunctival flap because of the safety it adds to the prevention of infection alone. Much of the criticism of the conjunctival suture is based on improper cutting of the flap, with the insertion of one suture, or not more than two, in a small pointed flap at the upper central part of the wound. I employ six to eight conjunctival sutures, placed in a flap which covers the entire incision, in most instances, from puncture to counterpuncture, so that the deep corneoscleral wound is completely covered. With this type of flap and method of suturing I have never seen the flap torn loose, with extrusion of vitreous, although slight separation of the edges of the deep wound is noted at times. This has apparently caused no trouble in most instances, the wound healing firmly after a few weeks.

TABLE 10.—*Visual Acuity in Five Hundred Cases in Which Intracapsular Extraction Was Performed*

Vision	No. of Cases		Percentage	Acuity
20/15	193			
20/20	153	413	82.6	20/30 or better
20/30	67			
20/40	19			
20/50	14			
20/70	11			
20/100	14	82	16.4	20/40 or less
20/200	13			
10/200-4/200	5			
Hand movements	4			
No vision	2			
Unknown	5		1.0	
	500			

RESULTING VISUAL ACUITY

Table 10 shows the record of visual acuity. Refraction is usually done six weeks after operation, when glasses are prescribed. However, in some instances the visual acuity recorded was the same as that noted after a brief refraction at the time of the patient's discharge, usually the

12. Kalt: Arch. d'opht. **21**:255, 1898; cited by Ellett, E. E.: Use of the Suture in Extraction of Cataract, Arch. Ophth. **17**:523 (March) 1937.

13. Liegard, cited by McLean, J. M., in discussion on Peter, L. C.: The Stallard Versus Multiple Conjunctival Sutures in Cataract Extraction, Tr. Am. Acad. Ophth. (1940) **45**:46 (Jan.-Feb.) 1941.

14. Stallard, H. B.: A Corneo-Scleral Suture in Cataract Extraction: Its Technique and Advantages, Brit. J. Ophth. **22**:269 (May) 1938.

15. Verhoeff, F. H.: Corneo-Sclero-Conjunctival Suture in Operations for Cataract, Tr. Am. Ophth. Soc. **25**:48, 1927; Instrument for Simplifying the Insertion of Corneo-Sclero-Conjunctival Sutures in Operations for Cataracts, Tr. Am. Acad. Ophth. **38**: 434, 1933.

16. McLean, J. M.: A New Corneoscleral Suture, Arch. Ophth. **23**:554 (March) 1940.

17. Recently I have been using buried catgut sutures to close the deep wound, combined with silk sutures for closure of the incision in the conjunctiva. (Davis, F. A.: Catgut Sutures for Closure of the Deep Corneoscleral Wound in Operations for Cataract: A Preliminary Report, Arch. Ophth. **31**:321 [April] 1944.)

fourteenth day, since some patients do not return to the clinic for final refraction.

As shown in table 10, in 413 (82.6 per cent) of the cases visual acuity of 20/30 or better was obtained, while in 82 (16.4 per cent) visual acuity was classified as 20/40 or less. Careful study of the records of the 82 cases in which final vision was less than 20/30 reveals that in 51 the poor acuity was apparently due to preexisting intraocular disease.

Table 11 briefly summarizes the data in the cases in which visual acuity was less than 20/30, with the diagnosis to which the lowered acuity

TABLE 11.—*Analysis of Cases in Which Visual Acuity Was Less than 20/30* *

		Total No. of Cases
Poor vision entirely or partly due to preoperative disease		51
Diabetic retinitis (2 with slight loss of vitreous)	14	
Chronic simple glaucoma (1 with loss of vitreous)	6	
High myopia	5	
Myopia with degeneration of vitreous (detachment 1½ years after operation)	1	
Senile macular degeneration	3	
Albinism with nystagmus	2	
Old corneal scars (interstitial in 1)	4	
Hypermature lens (15 years)	2	
Amblyopia (squint)	3	
Old retinal detachment (8 years)	1	
Chorioretinitis	2	
Retinitis pigmentosa	1	
Complicated cataract (old iritis with synechiae)	2	
Hypertensive retinitis, hemorrhage	2	
Juvenile cataract	1	
Polycythemia vera	1	
Subluxated lens (vitreous in anterior chamber, with slight loss)	1	
Poor vision attributed to postoperative complications		15
Hemorrhage into anterior chamber	4	
Hemorrhage into anterior chamber; loss of vitreous (fluid)	1	
Hemorrhage into anterior chamber and vitreous	2	
Keratoiritis	1	
Iritis, low grade; loss of vitreous, 4 drops	1	
Prolapse of iris	1	
Caught pillar	1	
Secondary glaucoma; bullous keratitis	1	
Corneal dystrophy	1	
Panophthalmitis (postoperative infection)	1	
Retinal detachment, 14 months after operation (original vision 20/15; small loss of vitreous)	1	
No cause of poor vision found; no complications		7
Patient did not return for refraction; visual acuity taken on fourteenth day		9
		82

* The 82 cases represent 16.4 per cent of the 500 cases in which intracapsular cataract extraction was performed.

was attributed. As will be noted, diabetic retinitis, chronic simple glaucoma and high myopia account for the lowered visual acuity in one-half the cases. In the remainder, poor acuity resulted from a variety of causes, as enumerated.

In 15 cases vision of 20/40 or less was attributed to operative complications, as shown in tables 11 (second part) and 12. In 7 of these cases postoperative hemorrhage into the anterior chamber or the vitreous was responsible for the lowered acuity. In 2 of the remaining 8 cases postoperative iritis was the cause, in 1 of which there was loss of vitreous. In 2 cases there were prolapse of the iris and an incarcerated pillar. In 1 case corneal dystrophy was present. In 1 case secondary glaucoma with bullous keratitis occurred. In 1 case retinal detachment developed fourteen months after operation.[18] Vision was 20/15 at the time of discharge and, according to the patient, remained excellent up to the time of the detachment. There had been a loss of about 3 drops of fluid vitreous at operation. A similar loss of fluid vitreous occurred in the fellow eye, but vision to date (five years after operation) has been 20/20 in this eye.

In the entire series, 1 eye was lost as a result of infection. The patient had pus cells in the smear, but, through carelessness, the resident house officer failed to report it to me. We have had only 1 other case of intraocular infection during this period; this was associated with an extracapsular extraction. The patient, inciden-

TABLE 12.—*Record of Visual Acuity in 15 Cases in Which Poor Vision Was Attributed to Postoperative Complications*

Vision	No. of Cases	Complication
20/40	2	Hemorrhage in anterior chamber
	1	Prolapse of one pillar of iris
	1	Caught pillar
20/50	1	Hemorrhage in anterior chamber
20/70	1	Hemorrhage in anterior chamber
	1	Loss of vitreous (fluid) and hemorrhage in anterior chamber
20/100	1	Hemorrhage in anterior chamber
	1	Keratoiritis
	1	Corneal dystrophy
20/200	1	Iritis, low grade, late; loss of vitreous
Hand movements	1	Hemorrhage in anterior chamber and vitreous
No vision	1	Retinal detachment (loss of vitreous) 14 months after operation
	1	Secondary glaucoma; bullous keratitis
	1	Panophthalmitis (postoperative infection)
	15	

18. Since this paper was written and the tables were compiled, a second instance of retinal detachment has been observed in a case of this series. It occurred three and a half years after operation, while the patient was shoveling coal.

During the past two years, in an additional 400 intracapsular operations performed since this series of 500 operations was reviewed, 3 additional cases of detachment have been encountered. Two occurred in 1 patient, in the first eye one year and in the second eye three months after operation. No vitreous was lost in either eye, and postoperative healing was prompt, with visual acuity of 20/30, maintained up to the time the detachments occurred. In the third case a detachment was noted one month after operation. The patient had pernicious anemia and suffered a cerebral vascular accident four months after the operation for cataract, while waiting in the hospital in preparation for an operation for reattachment of the retina. The operation was uncomplicated by either bleeding or loss of vitreous, and healing was prompt. Thus, we have had to date 5 cases of detachment in a series of 900 intracapsular operations, occurring three and a half years, one and a half years, one year, three months and one month respectively after operation.

tally, had had a successful intracapsular operation on the fellow eye four weeks before. He had chronic otitis media in one ear, of long standing, which had been brought under partial control by prolonged treatment in the department of otology. It is interesting that he escaped infection in the intracapsular operation but lost the other eye, operated on by the extracapsular method.

In 8 cases no definite cause could be found for the lowered visual acuity. In all cases the operation was without complication, and healing and the postoperative record were normal. Some of the patients spoke no English or other language that could be understood. Some were illiterate, and 1 patient was a malingerer and wanted a pension. There were not more than 4 cases in which loss of vitreous appeared to be the sole cause of poor visual acuity. In only 3 cases did secondary glaucoma develop.

A few other features deserve comment: In 1 case, that of a patient aged 82, scarlet fever with otitis media developed on the sixth postoperative day, with no interruption or complication in the healing process, and 20/20 vision was obtained. In another case mild otitis media developed. In 1 case erysipelas occurred on the seventeenth day, with no ocular complication and with final vision of 20/15 (Smith extraction). In 10 cases (possibly more) the patients were disoriented, in 2 so much so that their condition might be classed as postoperative mania. The disturbances in all cases cleared up promptly when the patch was removed from the fellow eye and the patient was allowed out of bed. In 1 case the patient fell out of bed on the eleventh day, breaking his hip; but his eye healed without complication, and vision was 20/15. In several cases restoration of the anterior chamber was delayed, in 1 case as late as the ninth day. Rest in bed and the use of a 2 per cent solution of pilocarpine hydrochloride daily was the only treatment employed, and in all cases healing occurred without further complication. In 2 of these cases delay appeared to be due to detachment of the choroid.

Failure of the deep wound to heal by first intention, with slight bulging of the wound under the conjunctival flap, was observed in a few cases, but, so far as I have been able to determine, in no case did actual postoperative prolapse or extrusion of vitreous occur. This indicates that a complete conjunctival flap with multiple conjunctival sutures will prevent rupture of the wound. The bulging under the flap proved to be due to aqueous in all but 1 case and usually disappeared by the twelfth to the fourteenth day. External oozing of thin serosanguineous fluid occurred in 3 cases, although the anterior chamber was not lost. No serious results followed except in 1 case, in which there was recurrent bleeding into the anterior chamber. No doubt a corneoscleral suture would prevent this separation of the edges of the deep wound.

True, or severe, iritis was observed in only 15 cases. No doubt there was a much larger number with mild irritation of the iris. However, when the patient was sent home on the fourteenth day with the ocular condition quiet, the postoperative reaction was not regarded, with rare exceptions, as iritis. In only 2 cases of iritis was the visual loss serious. In 1 of these cases, in which final vision was 20/100, there was severe keratoiritis, lasting three months. The patient had had no loss of vitreous. Similar iritis had followed an extracapsular extraction in the fellow eye, which was operated on elsewhere before the patient's admission to this clinic. The second patient had moderate loss of vitreous, with "hammock pupil," due to postoperative prolapse of the iris. Vision was 20/30 at the time of discharge, but a low grade iritis later developed, with reduction of vision to 20/200.

TABLE 13.—*Postoperative Iritis* *

Case No.	Vision	Time in Hospital	Comment
1	20/15	4 wk.	
2	20/15	39 days	
3	20/20	17 days	Mild iritis
4	20/200†	14 days	Vision 20/40 on discharge; "hammock pupil"; loss of vitreous
5	20/15	16 days	Low grade iritis
6	20/100†	3 mo.	Keratoiritis, severe
7	20/20	19 days	Low grade iritis; patient syphilitic
8	20/15	16 days	Late iritis, 1 month after discharge
9	20/30	20 days	Two drops of vitreous lost
10	20/15	30 days	Subluxated lens; no loss of vitreous
11	20/30	20 days	Low grade iritis
12	20/20	10 days	Mild iritis
13	20/20	3 wk.	Moderately severe iritis
14	20/30	3 wk.	Moderately severe iritis
15	20/20	20 days	Moderately severe iritis

* If the ocular condition was quiet and the patient was discharged within fifteen days, the case was not considered as one of true iritis, although in many instances postoperative irritation (low grade iritis) was present.

† Serious impairment of vision occurred in only 2 cases (4 and 6).

I am convinced that postoperative inflammation and iritis are much less frequently encountered with the intracapsular than with the extracapsular operation. This absence of postoperative irritation and inflammation in the great majority of cases is one of the most striking features of the intracapsular operation. Our record for postoperative vomiting coincides with that previously reported. It occurred occasionally when no postoperative sedative was used. We still avoid the use of morphine before or after operation, since it almost invariably produces vomiting. Codeine, ½ grain (30 mg.), and acetylsalicylic acid, 10 grains (0.6 Gm.), are the only sedatives used after operation, and they are avoided when possible. Pentobarbital sodium,

1½ grains (0.1 Gm.), is given by mouth one-half hour before operation.

The results of slit lamp studies, which were made before and after operation, differed little from those previously recorded.

Rupture of the hyaloid membrane, mushroom-like protrusions or strands were seen occasionally; also, holes in the hyaloid membrane were encountered at times. In 1 case a mushroom-like protrusion, without actual rupture of the hyaloid membrane, observed immediately after operation, has persisted unchanged for five years, with visual acuity of 20/20. In an occasional case a previously intact hyaloid membrane was observed to be ruptured, with extrusion of vitreous into the anterior chamber. Usually this was accompanied by no further complication, but in 1 instance low grade pain developed after this had occurred and persisted for some time. The first examination with the slit lamp after operation not infrequently revealed partial degeneration of the anterior portion of the vitreous. This was noted particularly in very old people. I have been unable to determine whether this condition existed before operation, and probably contributed to the development of the cataract, or whether it resulted from trauma incident to the extraction. This condition practically never interfered with healing, though visual acuity appeared at times to be affected by it.

Opacities in the deeper portion of the vitreous were commonly observed. Occasionally they were so pronounced that they interfered seriously with vision. The vitreous appeared to be fluid or partially degenerated in many of these cases. I assume that this condition existed some time prior to operation, though this could not be proved in all cases because of advanced changes in the lens on first observation. It was common in persons with high myopia. Pigment dust was frequently seen on the hyaloid membrane, and at times on the cornea.

In 2 cases pneumonia developed; 1 of the patients died, and the other recovered, obtaining 20/20 vision.

Records for astigmatism conformed closely to the average values observed after extracapsular operations. In this last series, of 300 cases, the average amount of astigmatism was 2.12 D. The highest was 5.50 D. (1 case), and the lowest, none (5 cases). No astigmatism was present in 5 cases; 1 to 2 D. of astigmatism, in 112 cases; 2 to 3 D., in 89 cases; 3 to 4 D., in 20 cases; 4 to 5 D., in 12 cases, and 5 to 6 D., in 1 case. There was no case of expulsive subchoroidal hemorrhage, although I observed this complication once during this period after an extracapsular extraction and once in a series of 400 additional intracapsular operations performed since the present series was reviewed.

COMMENT

The comments which conclude my former paper, based on the 200 cases reported at that time, need not be repeated here. Further experience with the additional series of 300 operations here recorded, as well as an additional series of 400 operations not yet reviewed, has served to convince me of the soundness of the intracapsular method of extraction. Once the technic is acquired, the operation is easier than the older method of capsulotomy, all things considered, at least in my hands. Loss of vitreous is no more frequently encountered, and need be no more common, than in the extracapsular operation. Healing in the majority of cases is far more rapid and attended with less complications than I have observed after the method of capsulotomy. Complications, of course, are inevitable in this, or in any other, method of operation, particularly when every patient is subjected to operation regardless of the outlook, so long as there is any hope of restoration of vision.

The technic of the operation as previously described has remained unchanged. My capsule forceps[19] were used in most of the operations, although the Arruga model is occasionally employed.

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19. Davis, F. A.: Capsule Forceps for Intracapsular Cataract Extraction, Tr. Am. Ophth. Soc. **34**:239, 1936.

CHANGES IN THE FUNDUS OF THE EYE IN VARIOUS FORMS OF ARTERIAL HYPERTENSION

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The following changes in the fundus of the eye may be observed in many cases of hypertension: (1) edema of the retina and the optic disk; (2) cotton wool patches; (3) hemorrhages; (4) sharply defined white spots in the deeper layers of the retina; (5) glistening white spots and a star-shaped figure in the macular area, and (6) changes in the retinal vessels.

The pathologic basis of these changes may be described as follows: (1) for the edema, transudation of fluid from the capillaries into the substance of the retina; (2) for the cotton wool patches, accumulations of precipitated fibrin and serum; (3) for the hemorrhages, the presence of blood in the various layers of the retina, especially in the inner layers; (4) for the sharply defined white spots, deposits of hyalin, mixed with lipids and with lipid-containing fat granule cells in the deeper layers of the retina, and for some of the more superficial white spots, a ganglioform swelling of segments of nerve fibers in the nerve fiber layer; (5) for the glistening white spots, deposits of lipid and lipid-containing fat granule cells, and for the star-shaped figure in the macular area, deposits of hyalin and lipids along the fibers of the layer of Henle, which radiate from the macula.

These changes in the vessels are of two kinds: (1) functional, resulting in contraction of the arteries, especially of the secondary and smaller branches, and (2) organic.

The organic changes in the vessels are due to the following factors:

(*a*) Aging of the vessels. This process results in diminution of the elasticity of the vessel wall and, therefore, in lengthening of the vessel and widening of its lumen. In the retina this shows itself in irregular tortuosity of the vessel and in widening of the light reflex on the surface of the vessel.

(*b*) Arteriosclerosis. This process causes irregular thickening and nodular deformation of the arterial wall. It reveals itself in the retinal arteries as irregularities in the lumen and as an apparent compression of the vein where it is crossed by an artery. This apparent compression of the vein has been shown, especially by the histologic studies of von Sallmann, to be due, not to an actual compression of the vein, but to thickening of the adventitial coats of the artery and of the veins and to thickening of the common connective tissue layer wherever there is one. Irregular tortuosity of the vessels, widening of the light reflex, irregularities in the lumen and apparent arteriovenous compression are signs of aging and of arteriosclerosis.

In addition, there are occasionally arteries which have a silver white appearance in various portions of their course—the so-caller silver wire arteries. This appearance is due to a deposit of hyalin beneath the endothelium in the intima of the artery. This change is illustrated by Ballantyne, Michaelson and Heggie.[1]

The changes which have been enumerated occur in many cases of hypertension. All these changes together appear only in some cases; in others some of them are present, and, again, in other cases perhaps none at all. Before their association with the various forms of hypertension is discussed, it is necessary to find the common factor in the pathogenesis of these alterations: the edema, the cotton wool patches, the hemorrhages, the deposits of hyalin and lipids and the narrowing of the arteries. The changes due to aging and arteriosclerosis need no further comment.

COMMON FACTOR IN THE RETINAL CHANGES

One can obtain an insight into the pathogenesis of these retinal changes by recalling the results of the studies on the terminal vessel units by Ricker and his school. It was observed experimentally that when contraction of a small artery was produced dilation of the terminal vessels—the precapillary arterioles, the capillaries and the postcapillary venules—occurred after a certain time. As a result, the circulation in these terminal vessel units is slowed, and when the arterial contraction above is complete, stasis results. When the contraction is not complete, stasis does not result, but slowing of the circulation and

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1. Ballantyne, A. J.; Michaelson, I. C., and Heggie, J. F.: Tr. Ophth. Soc. U. Kingdom (pt. 1) **58**:255, 1938.

diminution in the oxygen supply cause changes in the walls of the capillaries. At first the wall of the capillary becomes softened and permits fluid from the blood stream to pass into the tissues. Ricker spoke of this stage as peristasis. In a later phase temporary openings appear in the capillary wall and permit red blood corpuscles to pass through. This is the state of prestasis.

These principles in the general pathology of the blood vessels are exemplified in the retina in certain cases of hypertension, and the transudation of fluid and blood can be seen there as though produced experimentally. The narrowing of the arteries, the edema, the cotton wool patches and the hemorrhages indicate the occurrence of acute arterial contraction which is the result of dilation of the capillaries and the production of states of peristasis and prestasis. I shall speak of this condition as acute arteriospastic retinitis, or retinopathy. This, then, the arterial contraction, with the consequent dilation of the terminal vessel units, is the common factor in the pathogenesis of the visible retinal changes. When the arterial contraction is released, the arteries no longer appear narrowed, and the edema, the cotton wool patches and the hemorrhages gradually disappear. Such a process takes place, for example, in cases of acute diffuse glomerulonephritis with recovery.

When the arterial contraction persists for a sufficient time, the retinal tissue remains in a state of chronic deficiency of oxygen. Here, again, a fundamental principle of pathology finds expression in the visible changes in the retina. The deposits of hyalin and lipids and the star-shaped figure in the macular area are the result of the deficiency in the supply of oxygen, which, in turn, is due to the persistent contraction of the retinal arteries. I shall speak of this condition as chronic arteriospastic retinitis, or retinopathy. The ganglioform swellings of the nerve fibers in the nerve fiber layers have the same cause.

The acute and the persistent form of contraction occur in the retinal arteries in many cases of hypertension, in varying degrees. They account for the various combinations of narrowing of the arteries, edema, hemorrhages, cotton wool patches, deposits of hyalin and lipids and the star-shaped figure in the macular area. When the retinal vessels also show aging and arteriosclerosis, there are present, in addition, irregular tortuosity of the vessels, irregularities in the lumen and apparent arteriovenous compression.

VARIOUS FORMS OF HYPERTENSION

The various forms of hypertension may be classified as follows:

1. Essential hypertension in its benign phase.
2. Malignant renal sclerosis, or the malignant phase of essential hypertension.
3. Hypertension of renal origin.
   (*a*) Diffuse glomerulonephritis in its various forms (acute, subacute, subchronic and chronic).
   (*b*) In some cases of the more uncommon forms of renal disease, such as amyloid contracted kidney, unilateral renal hypoplasia, polycystic kidney, periarteritis nodosa with involvement of the vessels of the kidneys and hydronephrosis, pyelonephritis and prostatic obstruction.
4. Hypertension of preeclampsia and eclampsia of pregnancy.
5. Hypertension accompanying tumors of the adrenal glands and basophilic adenoma of the pituitary gland (Cushing's syndrome).

ESSENTIAL HYPERTENSION

Essential arterial hypertension is the form of hypertension that is most frequently encountered in the medical, as well as in the ophthalmic, clinics. In its clinical course the disease resembles chronic simple glaucoma. The latter condition begins to manifest itself in middle life, at the age of about 40, and occasionally earlier, with greater diurnal variations in the intraocular tension and with irregular periods in which the tension is increased. In time the greater diurnal pressures persist; the tension is high and does not return to normal without treatment, and eventually secondary changes occur in the eye. A similar course is seen in the cases of essential arterial hypertension. The normal arterial blood pressure is approximately 120 to 130 mm. of mercury, and 150 mm. is considered the upper limit of normal. In middle life, at the age of about 40, or slightly sooner, and occasionally at an early age, there occur greater diurnal variations of the blood pressure, and the pressure rises to 150 and 160 mm., only to return to normal at other times. With the passing of years the greater diurnal variations persist, but the blood pressure remains high, from 160 to 170 mm. In time it rises still higher, to 200 mm. and more, and finally persists at this level and cannot be reduced with treatment. Secondary arterial changes have now occurred.

Essential arterial hypertension also resembles chronic simple glaucoma in its essential nature. Glaucoma is a disease in which the physiologic mechanism for the maintenance of the intraocular tension, especially the central regulatory part of this mechanism, is inherently weak, and at middle

age, or earlier, it gradually loses its ability to maintain the normal intraocular tension.

Similarly, essential arterial hypertension is a disease in which the physiologic mechanism for maintenance of the normal blood pressure, especially the central regulatory part of this mechanism, is inherently weak as a result of hereditary influences and at middle age, or earlier, it gradually loses its ability to maintain the normal blood pressure. The hypertension is the central element of the disease. From the phase of the first greater diurnal variations in blood pressure to the period when the pressure remains permanently high, at 200 mm. or more, many years elapse—ten, fifteen or twenty years or more. It is for this reason that the disease is spoken of as benign hypertension. During the long early part of the period, in which the blood pressure gradually increases, no pathologic changes are present in the arteries anywhere in the body. The disease during this period is a definite functional one, an essential hypertension.

Such an increase in blood pressure can only be produced by the contraction of a large number of small arteries, and such a contraction occurs in the main effector organ for the maintenance of normal blood pressure, namely, the great vascular bed of the splanchnic region. Spastic contraction of the small arteries does not occur in any other organ in the body. This absence of spastic arterial contraction in such organs as the kidneys, brain, skin and eyes is of great importance, for it differentiates essential arterial hypertension, the benign form of hypertension, from other forms of high blood pressure.

It is obvious, therefore, that during the early years of essential hypertension there are no symptoms referable to any organ and no signs in the fundus of the eye which can be attributed to the hypertension. There is no spastic contraction of the retinal arteries, and therefore no signs of acute or chronic arteriospastic retinitis.

CHANGES IN THE LATER PERIOD OF BENIGN ESSENTIAL HYPERTENSION

In the later period of essential hypertension secondary changes, due to the persistent increase in blood pressure, manifest themselves in some arteries of the body. These changes occur practically always in the arteries of the kidneys and less frequently in those of the spleen, the pancreas and the brain. In the arteries of the kidneys there are observed (1) diffuse thickening of the intima of the smaller arteries, and (2) hyalinization with focal distribution of deposits of lipids in the smallest arteries, such as the terminations of the interlobular arteries and the afferent arteries of the glomeruli. This hyalinization and lipidosis of the prearterioles and arterioles in the kidneys give another name to the later phase of the benign form of essential hypertension, namely, renal arteriolosclerosis. These changes are much less frequent in the spleen and in the pancreas.

In the brain there occurs in the later stages of benign essential hypertension sclerosis of the larger vessels, especially those outside the brain proper. Within the brain, also, a subendothelial deposit of hyalin is focally distributed in segments of the small arteries. This hyalinization, which is also accompanied by deposits of lipids, corresponds to the arteriolosclerosis of the kidneys. When it occurs in the brain, the segment of the vessel is apt to form a miliary aneurysm, false or true, with eventual rupture and hemorrhages in the substance of the brain. This feature of essential hypertension has been studied especially by Spatz and his school. Such hyalinization occurs frequently, also, in the arteries of the choroid of the eye.

In the retina, as I have already mentioned, during the first period, of many years' duration, no changes referable to the hypertension are to be seen in the vessels, and of course none in the retinal substance. In the later stages, with the development of arteriolosclerosis in the kidneys and in the brain, there appear gradually in the vessels of the retina the changes due to aging and to arteriosclerosis, the production of which has been hastened by the chronic hypertension. There are then seen in the fundus angular tortuosity of the vessels, widening of the light reflex, irregularity of the lumen and apparent arteriovenous compression. Only rarely, and in the latest stage, does an occasional vessel show the white, "silver wire" appearance due to subendothelial hyalinosis.

The value to the physician of examination of the fundus of the eye in a case of the benign form of essential hypertension is primarily in the negative results. As long as there are only signs of aging and of arteriosclerosis in the vessels of the retina, and as long as there are no signs of acute and chronic arteriospastic retinitis, the disease is still in its benign form.

Complications.—However, complications may arise in the retina. The aging and the arteriosclerosis predispose the vessels of the retina to the following changes: (1) venous obstruction, more frequently of a branch, but occasionally also of the central vein; (2) obstruction of the central artery or of its branches, and (3) frequent or infrequent contractions of small arterial branches, with resulting small hemorrhages here and there in the fundus or with an occasional small area of edema or a cotton wool patch. The small vessels in the retina are especially liable to

occasional contractions in the course of essential hypertension in its later stages, and a few small, irregular hemorrhages, with an occasional cotton wool patch, are frequently seen in the retina in this stage. These are mild complications in the course of essential hypertension, but they point to a more important change.

I have said that acute and persistent spastic contraction of the retinal arteries does not occur in the benign form of essential hypertension. To this there are exceptions. In this disease, especially in the later stages, the arteries in many parts of the body are more labile and likely to undergo sudden contractions. This is particularly the case in the brain, where such sudden arterial contractions may give rise to temporary pareses and paralyses of the limbs, a possibility emphasized by Osler.[2] Frequently, such temporary pareses and paralyses are forerunners of permanent ones. In the retina, too, such arterial contractions are apt to occur in association with contractions of the cerebral vessels. When this happens, there appear in the retina the signs of acute and persistent spastic arterial contraction: namely, narrowing of arteries, edema, cotton wool patches, hemorrhages, deposits of hyalin and lipids and ganglioform swellings of nerve fibers. With the contraction of the cerebral arteries and the resulting edema in the brain there is increased intracranial pressure, with some swelling of the optic disks.

This change in the fundus is an added complication in the later stages of essential hypertension in some cases; when it is present, it places before the physician the problem of whether he is or is not dealing with the malignant form of essential hypertension. Continued observation alone can decide. When the occurrence of arteriospastic retinitis is only an episode in the late stage of benign essential hypertension, the spastic arterial contraction will recede under treatment. Also, the entire clinical picture must be taken into account. Episodal arteriospastic retinitis in the course of benign essential hypertension is not accompanied by any considerable renal insufficiency, and any renal insufficiency present will improve under treatment. Such episodes, however, foreshadow the eventual passing of the essential hypertension into a malignant stage, malignant renal sclerosis.

MALIGNANT RENAL SCLEROSIS, OR THE MALIGNANT PHASE OF ESSENTIAL HYPERTENSION

Essential hypertension in its ordinary, benign form lasts for decades, with relatively good health and normal renal function. Death is usually due to cardiac or cerebral disease or to an intercurrent disorder. In a number of cases, however, this phase passes into a malignant stage of hypertension. When this occurs, the clinical picture takes on the appearance of a new disease. This new hypertensive disease has been known by many names, such as malignant renal sclerosis, malignant hypertension, renal arteriolosclerosis with renal insufficiency and chronic hypertension with uremia. There is a fundamental difference between this form and the ordinary, benign form of essential hypertension. The malignant form is characterized by two important elements: (1) acceleration of the arteriosclerotic and arteriolosclerotic processes, especially in the kidneys, which led Klemperer to speak of this condition as the accelerated phase of essential hypertension, and (2) general arterial contraction, by which is meant that there is a persistent contraction of the small arteries, chiefly in the kidneys, but also in the spleen, pancreas, brain and eyes.

The acceleration of the arteriosclerotic and arteriolosclerotic processes is responsible for the occurrence of symptoms at an earlier age than with the ordinary, benign form. The acceleration may, according to Klemperer, possibly result from the arterial contraction, and is probably the cause of the severe changes in the large and small arteries in the kidneys, namely, the thickening of the intima, with its cellular and fibrous proliferation; the hyalin and lipid deposits, and the necrosis of the vessel wall, with nuclear disintegration and hemorrhages. The persistent arterial contraction in the kidneys is partly responsible for the renal insufficiency, and the contraction of the small arteries in the brain is responsible for the cerebral symptoms.

In the eyes, the persistent contraction of the small arteries is responsible for the changes in the retina. There are now apparent all the signs of arteriospastic retinitis: narrowed arteries, edema, cotton wool patches, hemorrhages, hyalin and lipid deposits and the star-shaped figure in the macular area. Edema of the optic disks is also present, due, first, to the contraction of the small arteries in the optic nerve and, also, to the increased intracranial pressure. Because the malignant stage of essential hypertension is preceded by a long period of high blood pressure, aging and sclerosis of the retinal vessels are also seen, with angular tortuosity of the vessels, irregularity of the lumen and apparent arteriovenous compression. The subendothelial hyalinosis is also observed in some of the arteries of the retina and gives the vessels their white, "silver wire" appearance.

2. Osler, W.: Canad. M. A. J. **1**:919, 1911.

These changes in the fundus of the eye, which are the result of aging, arteriosclerosis and acute and persistent contraction of the retinal arteries, are usually all present in cases of malignant renal sclerosis, or the malignant stage of essential hypertension. Variations in the fundic picture are due to variations in the individual factors. These changes when occurring in the presence of persistent renal insufficiency indicate a bad prognosis. Death is likely to occur within six months, occasionally later.

HYPERTENSION OF RENAL ORIGIN

In the hypertension which is the result of disease of the kidneys, the pathogenic factors differ from those of essential hypertension. In the latter, as I have previously stated, the hypertension is due to an inherited defectiveness of the mechanism for the maintenance of the normal blood pressure, especially of the central regulatory part of the mechanism. In hypertension of renal origin the central regulatory mechanism is also involved, but as a secondary and reflex effect from the kidneys. It will be recalled that a deproteinized plasma passes through the glomerular membrane by filtration, that for the purpose of filtration the kidney has an extremely sensitive pressure apparatus, that the force exerting the filtration pressure is the blood pressure and that when the blood pressure sinks to 40 mm. of mercury glomerular filtration ceases. The normal filtration pressure must therefore be maintained at all costs. It can be taken as a rule that whenever the normal glomerular filtration pressure is likely to be endangered, the organism responds at once with an increase in blood pressure. This is produced by a reflex from the kidneys over the central regulatory apparatus and by an arterial contraction effected by means of nerve impulses and hormones, such as renin or angiotonin. Such a danger to the normal intraglomerular filtration pressure occurs with diffuse glomerulonephritis in all its forms; in some cases of amyloid contracted kidney and polycystic kidney; in periarteritis nodosa when the renal vessels are affected, and in some cases of hydronephrosis, pyelonephritis and prostatic obstruction. Again, such a danger to the normal intraglomerular filtration pressure can be produced experimentally by narrowing of the lumens of the renal arteries, as has been shown by Goldblatt and his associates.

In all these forms of renal disease of which hypertension is a symptom there occurs contraction of the small arteries, which is usually general. It involves the small arteries of the kidneys, and probably those of other abdominal viscera and of the skin, brain and retina!

Glomerulonephritis.—In cases of acute diffuse glomerulonephritis the contraction of the small arteries in the skin is responsible for the pallor, and the sudden contraction of the small arteries in the brain is responsible for the headache, the convulsions and the occasional sudden loss of vision. In the retina the contraction of the arteries is shown by their narrowing, and with it are the signs of acute arteriospastic retinitis: edema, cotton wool patches and hemorrhages. The arterial contraction associated with acute diffuse nephritis is variable, with sudden steep rises and quick reductions in blood pressure. The pathologic features of acute arteriospastic retinitis are, therefore, also variable, the lesions varying from a few cotton wool patches and a few hemorrhages to the full blown picture. It may be recalled that acute diffuse glomerulonephritis is a disease of young people, and the signs of aging and of sclerosis of the retinal vessels are therefore not seen in such patients. The disease in its acute form does not last long, and in many cases recovery is complete. With recovery, the arterial contraction disappears; the blood pressure is reduced to normal, and all the signs of spastic retinitis disappear. When the disease is unusually prolonged, the signs of chronic arteriospastic retinitis, namely, deposits of hyalin and lipids and the star-shaped figure in the macular area, may be seen. These lesions, too, disappear with recovery. The changes in the fundus have practically no prognostic value with this condition. They signify only that the arterial contraction is also present in the retina and that it is either of short or of long duration.

With the subacute form of diffuse glomerulonephritis, which may last six months, and the subchronic form, which may last as long as two years, there appear in the fundus of the eye varying signs of acute and chronic arteriospastic retinitis. These signs differ with the degree and the duration of the arterial contraction and with the frequency of its recurrence in an acute form.

The chronic form of diffuse glomerulonephritis lasts from a few years to over twenty years. It is characterized by periods in which the disease is quiescent and the blood pressure either high or low, but stationary, and by periods of recurrent acute attacks. All possible combinations of the signs of acute and chronic arteriospastic retinitis may be seen in the course of the disease. With the passing of years the signs of aging and of sclerosis of the retinal vessels are added. In the advanced stage of the disease, with high blood pressure, renal insufficiency and the full blown picture of acute and chronic spastic retinitis, differentiation between this disease and

the malignant stage of essential hypertension may be difficult. The fundus picture alone is not sufficient to differentiate the two. In the case of either disease, when renal insufficiency is present the changes in the fundus indicate a poor prognosis, but the physician is aware of the poor outlook without knowing anything about the fundus.

It is of interest to remember that in many cases of chronic diffuse glomerulonephritis the disease may be present a long time, until termination, without hypertension. In such cases there is no arterial contraction in the brain or in the eyes. Examination of the fundus shows normal arteries and no signs of either acute or chronic arteriospastic retinitis.

Other Forms of Renal Disease.—Such conditions are not always accompanied by an increase in blood pressure. When hypertension is present, the symptoms, including the changes in the fundus, are those occurring in the course of chronic diffuse glomerulonephritis.

HYPERTENSION ASSOCIATED WITH PRE-ECLAMPSIA AND ECLAMPSIA OF PREGNANCY

In the clinical picture of preeclampsia of pregnancy hypertension is the chief symptom. This hypertension is not produced reflexly from the kidneys but is due to increased irritability of the regulatory center of the mechanism for the maintenance of normal blood pressure. The increased irritability of this regulatory center is an unwelcome secondary effect in some cases of pregnancy, and it lasts as long as there is increased irritability of the regulatory mechanism for uterine contractions. As a result, there is acute spastic contraction of the small arteries in many organs: the kidneys, other abdominal viscera, the skin, the brain and the eyes. The arterial contraction in the kidneys is responsible for the renal symptoms, and in the brain it produces the headache and the sudden amaurosis which occurs occasionally. The arteriospastic contraction is extremely variable and is liable to sudden changes. Sudden acute arterial contractions result in explosive symptoms, such as the convulsions which give eclampsia its name.

In the fundus of the eye the contraction of the arteries is shown by the narrowing of the vessels, which manifests considerable variability. The arterial branches are narrowed throughout their length, or segments of narrowing may alternate with segments of normal caliber. Dependent on the degree of arterial contraction, there are signs of acute arteriospastic retinitis: edema of the retina, cotton wool patches and hemorrhages. These, too, are variable, and only a few cotton wool patches and a few hemorrhages may be seen. Occasionally the retinal edema is of considerable extent, and the transuded fluid seeps through into the subretinal space and lifts up the retina. Preeclampsia is usually not permitted to exist for any length of time, and the symptoms of the more chronic arterial contraction, the hyalin and lipid deposits and the star-shaped figure in the macular area, are therefore not ordinarily observed. In rare cases they may be noted.

The changes in the fundus of the eye indicate the severity of the arterial contraction. As a guide to the advisability of artificial termination of the pregnancy the ocular changes are of less importance than the continuous observation of the state of the blood pressure.

The increased irritability of the regulatory center disappears with the cessation of the uterine contractions. With the complete involution of the uterus, all the signs in the fundus of the eye recede, with the other symptoms of preeclampsia and eclampsia.

HYPERTENSION WITH TUMORS OF THE ADRENAL AND THE PITUITARY GLANDS

Tumors of the Adrenal Gland.—Such tumors are rare. The clinical picture is characterized by paroxysmal attacks of blanching of the skin, palpitation, tachycardia, dyspnea and increase in blood pressure. The symptoms are due to an increased secretion of the hormones of the gland, which also produce arterial contraction in many organs, including the retina. The arteriospastic retinitis thus produced is said to resemble at times that of malignant renal sclerosis.

Basophilic Adenoma of the Pituitary Gland (Cushing's Syndrome).—This syndrome is characterized chiefly by adiposity, profuse growth of hair, plethoric appearance of the face, purplish red striae in the skin of the abdomen, the hips and the thighs, sexual dystrophy, polycythemia, osteoporosis of the skull and spine and arterial hypertension. The hypertension resembles that associated with adrenal tumors. It is possible that the increased production of hormones of the pituitary in cases of basophilic adenoma of this gland acts by increasing the production of hormones of the adrenal gland. In the 1 case of Cushing's syndrome which I had occasion to study there were no retinal changes. It is of course possible that with general arterial contraction an arteriospastic retinitis may be produced in this disease.

SUMMARY AND CONCLUSION

The changes in the retina which occur with the various forms of hypertension depend (1) on the contraction of the retinal arteries and (2)

on the degree and extent of their aging and arteriosclerosis.

Dependent on the persistence of the arterial contraction, the changes in the retina can be separated into acute arteriospastic retinitis, or retinopathy, characterized by edema, cotton wool patches and hemorrhages, and a more chronic arteriospastic retinitis, or retinopathy, characterized by deposits of hyalin and lipids and by the star-shaped figure in the macular area.

In uncomplicated essential hypertension in its benign form the retinal arteries are not contracted. The changes in the fundus of the eye are only those of aging and sclerosis of the retinal vessels. In the later stages occur complications, such as a few hemorrhages, occasionally a few white spots and occlusion of branches of the central vein and artery, occasionally of the main vessels as well. A more important complication is temporary arteriospastic retinitis, as part of a temporary arterial contraction in many organs. The clinical picture can be differentiated from that of the malignant stage of essential hypertension by the absence of any severe renal insufficiency.

In other forms of hypertension the fundus presents varying combinations of the signs of acute and chronic arteriospastic retinitis and of aging and sclerosis of the retinal vessels.

DISCUSSION

Dr. Herman Mosenthal, New York: Dr. Elwyn's paper has been one of the most comprehensive and appealing presentations that I have ever heard on the subject of morphologic changes in the eyegrounds associated with hypertension. I shall confine my discussion to the functional changes involved. One should recognize that there is no uniformity of opinion concerning the interpretation of the functional pathology of hypertension. Undoubtedly, there is spasm, or, more precisely, increased tonicity, of the arterioles and of the larger arteries when the blood pressure is elevated. A vexing question in this connection is whether the so-called spasm of the arterioles, resulting in "peripheral vasoconstriction," is the cause of or is secondary to the hypertension. The accepted idea is that it is the cause.

It is thought that the arterioles act as stopcocks to draw on the arterial pressure and regulate the supply of blood flowing to the capillaries. In all the organs that have been studied, that is, the kidney, brain, lung, skin and muscle, it is known that the arterioles do not maintain a constant diameter but that they distend and contract —even to the point of closure—in accordance with the physiologic needs of the tissue the blood supply of which they control. Also, the arterioles do not dilate and contract throughout the body as a whole but differ widely in this regard with each tissue. For instance, during a chill the blood vessels of the skin contract to a remarkable degree, while those in the deeper organs dilate. The same is true of exposure to cold. The blood supply also varies enormously with the activity of individual organs. This probably has been shown best by Richards, who observed that in the kidney as few as 5 per cent of the afferent glomerular arterioles may be open when the kidney is at rest and that 95, or even 100, per cent may be open when diuresis is produced. In view of all these observations, it seems illogical to assume that peripheral vasoconstriction involving the entire body is the cause of hypertension; rather, it is likely that the hypertension is produced elsewhere and that the peripheral vasoconstriction is secondary to the high blood pressure and serves the hypertensive person in the same way that it does the normal person, namely, to control the amount of blood flowing to the tissues so that normal function may proceed.

Medicine offers several good illustrations in support of the theory that constriction of the perpheral vessels is secondary to the degree of blood pressure which exists in the larger arteries. After the subtotal sympathectomy now in vogue for the cure of hypertension, it is found that the blood vessels of the retina dilate and assume a normal caliber, even though the sympathetic supply to the vessels of the eye is not severed. In other words, the lowering of the blood pressure due to the effect of sympathectomy on vessels in the body not involving the eye has brought about an adjusted physiologic dilation of the blood vessels of the retina, evidently in an effort to maintain a normal blood flow under the circumstances. It has been amply demonstrated that hypertensive retinopathy can be cured by subtotal sympathectomy and that the condition remains quiescent as long as the blood pressure is not elevated.

Another good example in support of the same interpretation, namely, that contraction of the arterioles is secondary, not primary, to the hypertension, is seen in cases of coarctation of the aorta, in which the pressure rises in the arms and in the head; this elevation of arterial pressure is, in all probability, due to narrowing of the aorta. (The enthusiasts who insist on ascribing all hypertension to renal ischemia point to the fact that the blood pressure also rises in the legs. The blood pressure in the legs, however, rises in a different fashion than it does in the arms. In the arms there is an increase in both the systolic and the diastolic pressure, while in the legs there is a rise in the diastolic, and not in the systolic, pressure. In other words, the pressure in the legs is the type characteristic of diminishing circulation, such as that associated with cardiac failure, the decreased blood supply to the legs being readily explained by the narrowed aorta.) The effect of the high arterial pressure on the peripheral vessels in the arms is constriction of the arterioles, so that capillary circulation is

maintained at a normal rate. In this instance the arterioles contract in response to hypertension, and are not the cause of it. This, again, illustrates how the musculature in the arterioles regulates the blood flow in the peripheral circulation and maintains it at a constant level regardless of the level of the arterial pressure.

Another illustration of the same mechanism is found in cases of extensive coronary thrombosis. In this condition the blood pressure drops for the undeniable reason that the heart is weaker than it was before the impairment. The decrease in blood pressure may be exceedingly great; yet in most cases the circulation in the periphery is maintained in normal fashion, evidence that the peripheral vessels dilate to accommodate themselves to the diminished arterial pressure and to allow a normal supply of blood to the capillaries. To put it in another way, contraction or dilation of the arterioles is a regulatory mechanism which accommodates itself to the rise or fall of the systemic arterial pressure.

That an increase in blood pressure causes the morphologic changes in the arterioles and in the larger blood vessels has been convincingly demonstrated by Goldblatt. He produced narrowing of both renal arteries and observed that the changes of necrotizing arteriosclerosis, which are the true signs of malignant hypertension, were present in all organs but the kidneys. The hypertension in this experiment made itself felt in all the blood vessels except those of the kidneys, where the blood pressure was not elevated because of the narrowing of the main renal arteries. Ordinarily, the kidney is one of the most vulnerable organs of the body in its reaction to hypertension, and the fact that it did not exhibit any changes in this experiment is conclusive evidence that the mechanical effect of the hypertension is responsible for the arterial and arteriolar changes which are common in cases of essential or renal hypertension in human beings.

239 Central Park West.

NERVOUS FACTOR IN THE ORIGIN OF SIMPLE GLAUCOMA

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In another paper [1] we have stated that in cases of clinically unilateral simple glaucoma pupillary disturbances may generally be detected in the seemingly unaffected eye. These disturbances were found to be based on three factors: (1) modifications of the retinal receptors, (2) damage to the effector organs and (3) lesions in the central nervous system.

While in the early stage of the disease the first two factors were not constant, the third factor was always present. On the basis of new experiments, we shall discuss in this paper the origin and significance of the nervous factor. Is this factor sympathetic or parasympathetic, central or peripheral? Our studies were made both in cases of unilateral simple glaucoma, in which increase of tension has not yet occurred in the unaffected eye, and in cases of well developed glaucoma, both unilateral and bilateral.

RÉSUMÉ OF PREVIOUS STUDIES

Before analyzing the pupillary reactions to light characteristic of glaucoma, we shall recapitulate briefly some results of former pupillographic studies.[2] It is known that both the contraction to light and the redilation following it consist of various stages. The contraction begins after a latency period of 0.2 to 0.3 second; latency periods longer than this are considered pathologic. The period of contraction consists of three phases:[3] (1) a primary phase of about 0.4 second and an average speed of about 5 mm. per second (fig. 1 *a* to *b*); (2) a secondary phase of about 0.3 to 0.4 second and an average speed of about 2 mm. per second (fig. 1 *b* to *c*), and (3) a tertiary phase, which is variable, of about 0.3 to 0.5 second and an average speed of 0.8 to 1.9 mm. per second (fig. 1 *c* to *d*).

The phase of redilation consists of a latency period, which is about equal to the latency period for contraction, a preliminary phase of dilation (fig. 1 *d* to *e*), and then a primary, (fig. 1 *e* to *f*), a secondary and a tertiary phase.

The light reflex of the pupil is usually considered parasympathetic. However, some features of the phases of contraction, particularly the secondary and the tertiary phase, are determined by the functional state of the sympathetic system, whereas the primary phase of contraction depends predominantly on the parasympathetic. Evidence for this is found in the fact that instillation of cocaine into the conjunctival sac improves the secondary and tertiary phases of the contraction period of the light reflex in cases in which these phases are poor. The primary phase of contraction of the light reflex directly expresses the influence of the third cranial nerve. A certain functional sympathetic tone is necessary to bring about not only a maximal sympathetic response, such as the psychodilation reflex, but a maximal parasympathetic response, such as the light reflex.

Poor sympathetic innervation facilitates the occurrence of symptoms of fatigue in the pupillary light reflex, and these sympathetically conditioned symptoms are characterized by gradual

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Pupillographic Studies: VII. From the Departments of Neurology and Ophthalmology, New York University College of Medicine.

This paper, in abbreviated form, was read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, on Jan. 17, 1944.

1. Lowenstein, O., and Schoenberg, M. J.: Pupillary Reactions of the Seemingly Unaffected Eye in Clinically Unilateral Simple Glaucoma: Pupillographic Contributions to the Diagnosis of Glaucoma in the Preclinical Stage, Arch. Ophth., this issue, p. 392.

2. (*a*) Lowenstein, O., and Friedman, E. D.: Pupillographic Studies: I. Present State of Pupillography; Its Method and Diagnostic Significance, Arch. Ophth. **27**:969 (May) 1942. (*b*) Lowenstein, O., and Levine, A.: Pupillographic Studies: V. Periodic Sympathetic Spasm and Relaxation and Role of Sympathetic Nervous System in Pupillary Innervation, ibid. **31**:74 (Jan.) 1944. For a better understanding of the principles applied in the present paper, the second article in particular should be referred to.

3. Gradle, H. S., and Ackerman, W.: Reaction Time of Normal Pupil: Second Communication, J. A. M. A. **99**:1334 (Oct. 15) 1933. The authors found a latent period of 0.1875 second. They detected a primary and a secondary (not a tertiary) phase of contraction, the former lasting 0.4365 second, with a rate of contraction of 5.48 mm. per second, and the latter lasting 0.3125 second, with a rate of 1.34 mm. per second.

fatigue diminution and early disappearance of the secondary and tertiary phases of contraction. However, another type of fatigue exists, due to damage to the nucleus of the third nerve; this is manifested, first, as an initial dilation preceding the contraction to light, and second, as an inhibition of the primary phase of contraction, which becomes sluggish. In cases of poor sympathetic innervation there develop hypersensitivity to cocaine and hyposensitivity to physostigmine, and in cases of hyperstimulation of the sympathetic fibers, hypersensitivity to physostigmine and hyposensitivity to cocaine. When the reflex to light is elicited by a weak stimulus, affecting only a relatively small number of retinal receptors, the first phase of contraction diminishes in extent (fig. 1 *B*, *a'* to *b'*).

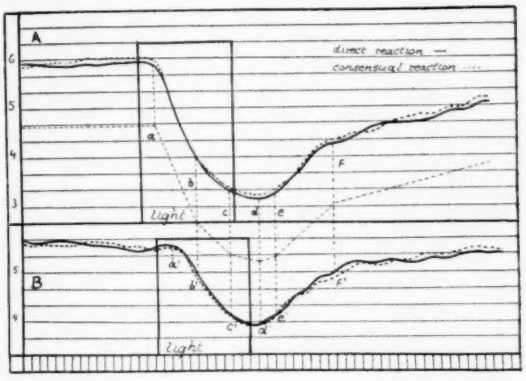

Fig. 1.—Influence of graded intensities of light stimuli on the different phases of contraction in a normal man, aged 53.

A, reflex to light elicited by a light stimulus of average intensity. A normal reflex is elicited, consisting of three phases of contraction (broken middle line): *a* to *b* indicates primary phase of contraction; *b* to *c*, secondary phase of contraction, and *c* to *d*, tertiary phase of contraction.

B, reflex to light elicited in the same subject by a light stimulus of low intensity (just visible).

All three phases of contraction are present: the primary phase, from *a'* to *b'*; the secondary phase, from *b'* to *c'*, and the tertiary phase, from *c'* to *d'*. While distance *b'* to *c'* is equal to distance *b* to *c*, and distance *c'* to *d'* to distance *c* to *d*, the primary phase (*a'* to *b'*) is only about one-fourth distance *a* to *b*. That is, differences in the intensity of the light stimulus produce differences in the primary phase of contraction but not in the following phases.

The latency period in *B* is slightly longer than that in *A*.

REPORT OF REPRESENTATIVE CASES

We distinguished four groups of cases; for every group a representative case is described.

First Group (fig. 2).—Case 1 (A. S.): This case is the same as case 2 of "Pupillographic Studies: VI."[1] In figure 2 are shown the reactions to light when the right, clinically normal, eye is stimulated, the left eye reacting consensually.

First Reaction: The first reaction, occurring after a latency period of less than 0.3 second, was nearly normal, although somewhat sluggish in all its phases. The primary contraction amounted to about 1.7 mm. in 0.4 second, the average speed being 4.2 mm. per second, instead of the normal rate of about 5 mm. per second. The secondary and tertiary phases of contraction together amounted to 0.6 mm. in 0.7 second, the average speed being 0.9 mm. per second, instead of the normal rate of 1.6 mm. per second. The spatial relation of the contraction of the pupil during the primary phase as compared with the contraction during the combined secondary and tertiary phases was about 3:1 (normal, 2:1). The ratio of the average speeds of contraction was about 4.6:1 (normal ratio, 3:1).

Second Reaction: But in the second reaction the ratio of the extent of the contraction in the primary phase to that in the secondary and tertiary phases increased to 8:1. The secondary and tertiary phases were practically absent, and this was still more noticeable in the third reaction to light.

In the third reaction to light the latency period increased to more than 0.3 second and was replaced by a slight initial dilation. At the same time, the speed of contraction in the primary phase was also decreased, but far less so than that in the secondary and tertiary phases. (In the second reaction the speed was 1.3 mm. in 0.4 second, or an average speed of 3.2 mm. per second, and it was still a little less in the third reaction.)

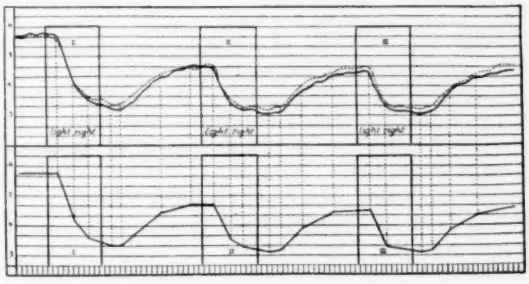

Fig. 2 (group 1).—Latent glaucoma in the supposedly unaffected right eye in a case of so-called unilateral simple glaucoma of the left eye.

First line: Three reactions of the right pupil to the light. The solid line indicates the direct reaction, and the broken line, the consensual reaction.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction to light: The three phases of contraction are present. The ratio of the amount of the primary phase of contraction, on the one hand, to that of the secondary and tertiary phases, on the other, is about 5:3.

Second reaction to light: The secondary and tertiary phases of contraction show a tendency to disappear but are still visible.

Third reaction to light: The primary phase of contraction is present to the same degree as that in the first and second reactions to light. A secondary and a tertiary phase are no longer distinguishable. The third reaction appears as though it were cut off at the end of the primary phase of contraction.

This case is characterized by the normal, although somewhat sluggist, first reaction of the pupil of the clinically unaffected eye to stimulation by light. The relation of the primary phase of contraction, on the one hand, to the secondary and tertiary phases, on the other, was also nearly normal. However, under the influence of repeated light stimuli, a disproportion quickly developed, so that in the second reaction to light the secondary and tertiary phases of contraction were practically absent, while the primary phase of contraction was comparatively only slightly fatigued.

Second Group (fig. 3).—CASE 2 (S. H.): This case is identical with case 1 in "Pupillographic Studies: VI." [1]—an instance of simple glaucoma in which clinically only the left eye was affected. We emphasized in that paper that pupillographic studies revealed that the right eye was also affected. In figure 3 are

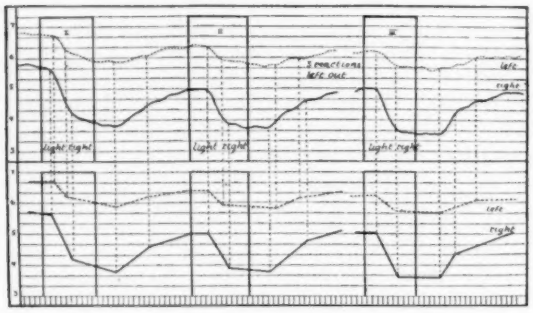

Fig. 3 (group 2).—Latent glaucoma in the supposedly unaffected right eye in a case of so-called unilateral simple glaucoma of the left eye.

First line: First, second and sixth reactions in a series of stimulations of the right pupil by light.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction: The secondary and tertiary phases of contraction are undistinguishable. The ratio of the contraction in the first phase to that in the following phases is about 4.5 : 1.

Second reaction: The secondary and tertiary phases of contraction are nearly absent.

Sixth reaction: The secondary and tertiary phases of contraction are entirely absent. The primary phase of contraction is practically unchanged.

analyzed the pupillary reactions of both eyes, when the right eye was stimulated by light and the left pupil responded consensually.

First Reaction: It can be seen that the first phase of contraction was present, although somewhat sluggish. In the right pupil the contraction amounted to about 1.45 mm. in 0.35 second—an average speed of 4.1 mm. per second, instead of the normal rate of about 5 mm. per second. This phase was followed by a secondary and a tertiary phase, which together amounted to only 0.4 mm. in 0.9 second—an average speed of only 0.44 mm. per second, instead of a normal contraction of 1 mm. in about 0.6 second, or an average speed of 1.6 mm. per second.

The ratio of the change of diameter in the primary phase to that in the combined secondary and tertiary phases was about 4 : 1 (normal 2 : 1). The ratio of the average speeds in the phases under comparison was 9.3 : 1 (normal, 3 : 1).

Second Reaction: This ratio was further decreased in the second reaction to light, in which the secondary and tertiary phases of contraction were practically absent (0.1 mm. in 0.9 second), while the primary contraction amounted to 1.1 mm. in 0.3 second—an average speed of 3.6 mm. per second.

Other Reactions: The latency period for contraction, which was less than 0.3 second in the first reaction to light, had already increased to more than 0.3 second in the second reaction and had been replaced by an initial dilation in the fourth reaction. The fifth reaction, after a psychosensory stimulus which was interposed between the fourth and the fifth reaction, showed a slight degree of restitution, while the sixth reaction, again, showed complete absence of the secondary and tertiary phases of contraction.

In this case in the clinically normal eye there existed a disproportion between the primary phase of contraction, which was comparatively well developed, on the one hand, and the secondary and tertiary phases, which were poorly developed, on the other. This disproportion between the first and the subsequent phases of contraction increased under the influence of repeated stimulation with light. The speed of the primary phase of contraction was somewhat diminished. The latency period was increased in the first reaction to light, and an initial dilation preceded contraction as early as the fourth reaction to light. The secondary and tertiary phases were poor and had almost disappeared in the second reaction to light. While the disorders of the primary phase of contraction which occurred under the influence of repeated stimulation by light were relieved by psychosensory restitution, the disorders of the secondary and tertiary phases remained. The sixth reaction, for example, showed that, while the latency period was less than 0.3 second and the primary contraction amounted to 1.4 mm. in 0.4 second, with an average speed of 3.5 mm. per second, the secondary and tertiary phases of contraction were completely absent.

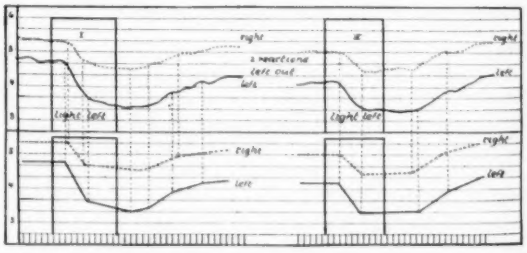

Fig. 4 (group 3).—Bilateral simple glaucoma, present to a higher degree in the right eye than in the left.

First line: First and fourth pupillary reactions of the left eye to light.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction: The secondary and tertiary phases of contraction are undistinguishable. The ratio of the first phase to the following phases is 3.5 : 1 in the direct reaction. For the consensual reaction of the right pupil the ratio is 2 : ⅓.

Fourth reaction: The secondary and tertiary phases of contraction are absent. The primary phase of contraction is somewhat diminished and more sluggish, as compared with the primary phase of the first reaction. Note the slight tendency to negative (reversed) secondary and tertiary phases of contraction, i. e., a slight dilation, instead of contraction, in the consensually reacting right pupil in the fourth reaction.

Third Group (fig. 4).—CASE 3: M. B. S., a woman aged 64, stated she had always been nervous, easily upset and easily depressed and that she had slept poorly over since she was in college.

In October 1940 she had an attack of severe pain in the eyes, without blurring of vision or the seeing of rainbows. Two months later tonometric examination revealed a notable increase of intraocular pressure (35 mm., Schiøtz) in both eyes. Pilocarpine nitrate, in 0.5 per cent solution, reduced the pressure by 15 mm.

Neurologic examination showed overactivity of the deep reflexes, particularly the patellar responses and the reflexes of the upper extremities, but no organic factors were involved. Examination of the eyes revealed the characteristic signs of simple glaucoma. There were slight pallor and partial cupping of the right optic disk and slight pallor and shallow cupping of the entire left optic disk.

Perimetric examination showed paracentral defects. Repeated studies showed a tendency to enlargement of the scotoma.

Intraocular pressure was 30 mm. in the right eye. In the left eye it measured 28 mm. (Schiøtz) with a 7.5 Gm. weight, after use of a miotic had been discontinued for twenty-eight hours.

Vision was 20/15 + + in both eyes, correction with a + 2.50 D. sphere being prescribed for each eye.

On April 4, 1941, iridencleisis was performed on the right eye, and on May 12, on the left eye. Thereafter the intraocular pressure in the left eye remained normal (without the use of a miotic), while in the right eye it had a tendency to rise to 25 or 30 mm. This increase in pressure, however, responded to administration of prostigmine methylsulfate, 0.5-1 per cent.

There was slight anisocoria, the right pupil measuring 5.5 and the left pupil 4.85 mm. The contraction of the right pupil amounted to 0.6 mm. and remained at about the same level in the following five reactions.

The reaction of the left pupil to the first stimulus amounted to 1.3 mm., and in the following reactions the contraction was a little less than 1 mm.; the reaction to light after a sound stimulus was 1 mm. The latency period was more than 0.3 second in the first reaction and in all the subsequent reactions. The primary contraction of the left pupil to light, while the right pupil reacted consensually, amounted to 1.1 mm. in 0.4 second, with an average speed of 2.75 mm. per second; the secondary and tertiary contractions amounted to 0.25 mm. in 0.6 second, with an average speed of 0.4 mm. per second. The secondary and tertiary phases of contraction were almost absent in the second reaction and entirely absent in the fourth reaction. The ratio of change in pupillary diameter in the primary phase of contraction to that in the secondary and tertiary phases was 4.5:1. The psychosensory restitution increased the amount of the primary phase of contraction, but not of the secondary and tertiary phases, and produced a sort of initial dilation.

The reaction of the right eye to light, while the left one responded consensually, did not show a secondary or a tertiary phase of contraction, even at the beginning. The latency period was more than 0.3 second. The primary phase of contraction, which was already sluggish, amounted to 0.6 mm. in 0.6 second, or an average speed of 1 mm. per second.

Fourth Group (fig. 5).—CASE 4: L., a physician, stated that since 1919 he had been suffering from glaucoma. He had had continuous headaches for many years but no fits. An operation (trephination) was performed in 1927 on both eyes, and a second operation, on the left eye, was done in 1935.

Neurologic examination showed that the deep reflexes were hyperactive, those on the left being slightly more active than those on the right.

The pupillographic picture showed that the diameter of the right pupil was 2.15 mm. and that of the left pupil 2.6 mm. The right pupil showed a latency period for contraction to light of more than 0.4 second. The primary phase of contraction of the right pupil was sluggish and inextensive, amounting to 0.3 mm. in 0.4 second (0.75 mm. per second), and that of the left pupil was 0.3 mm. in 0.6 second (0.5 mm. per second). The secondary and tertiary phases were completely abolished.

COMMENT

Analysis of the pupillary reflex to light in cases of simple glaucoma reveals certain constant characteristics. In cases in which clinically the disease is not yet well developed, or is not developed at all, as, for instance, in the supposedly unaffected eye in a case of unilateral glaucoma, the first symptom to be noted is a disproportion between the primary phase of contraction, on the one hand, and the secondary and tertiary phases,

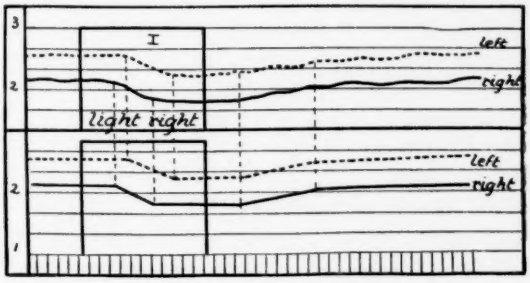

Fig. 5 (group 4).—Bilateral glaucoma, with small pupils and anisocoria.

First line: Reflex of the right pupil to light, the left pupil reacting consensually.

Second line: Scheme of the reaction, showing the phases of contraction and redilation.

The secondary and tertiary phases of contraction are absent. The primary contraction is greatly diminished, being inextensive and sluggish.

on the other. This disproportion is characterized by the preservation, to a greater or less extent, of the primary phase and the significant decrease, both in extent and in speed, of the secondary and tertiary phases.

In certain cases of incipient or preclinical glaucoma the disproportion described is not yet present in the first reaction elicited by stimulation with light, but appears in the second, or even in the third, reaction, by which time a certain degree of fatigue has been attained (group 1). As the severity of the glaucoma increases, this disproportion, too, increases and is finally demonstrable in the first reaction to light (group 2). In the further development of the glaucomatous process, a third type of pupil-

lary reflex appears; in this response, the disproportion has further increased, and the primary phase of contraction has gradually become sluggish, while the latency period preceding contraction has increased, or has even been replaced by an initial dilation (group 3). In some cases, however, sluggishness of the primary phase and an increase in the latency period are present at a very early stage. But it may be stated that, in general, when the primary phase of contraction has become sluggish and the latency period is over 0.3 second, the secondary and tertiary phases of contraction have completely, or almost completely, disappeared (group 4). At that time the full characteristics of the light reflex of the glaucomatous pupil are present, i. e., a sluggish and inextensive pupillary movement, beginning after a long latency period (from 0.4 to 0.6 second), the primary phase of contraction being no longer followed by secondary and tertiary phases.

In another paper on glaucoma,[1] we discussed the reasons for our belief that damage both to the central nervous system and to the eyes produces the abnormalities present in the pupillary reflexes to light. We expressed the opinion that one is justified in the assumption that the lesions in the central nervous system are primary, although damage both to the effector organs and to the retinal receptors appears to be essential to an explanation of the pupillary picture in the final stages. However, we were unable to answer the question whether the peripheral lesions are secondary to the increase of intraocular tension or are simply associated with it; such an association would mean that all damage is the immediate and coordinate expression of the lesion in the central nervous system, perhaps through the mediation of the blood supply.

The high degree of sluggishness in the primary phase of contraction has been attributed to damage in the effector area, and the decrease in the extent of the primary contraction phase to retinal damage. Since we observed a number of cases of unilateral glaucoma in which no increase in intraocular tension had been observed in the unaffected eye, but in which nevertheless the pupillary light reflex showed typical glaucomatous modifications, the conclusion appears justified that intraocular tension is not responsible, or at least not solely, for the development of the glaucomatous type of reaction to light.

Another observation points to the same assumption.

A physician aged 49 had had a cyclodialysis performed on both eyes six years previously. Since the operation his right eye had remained hypotensive; the tension in the left eye had tended to rise to 35 mm. or more, but could be kept under control by the administration of pilocarpine. Pupillographic examination in this case revealed a characteristic disproportion between the primary phase of contraction and the following phases, which were almost absent, or at least greatly decreased. These characteristics were present in the responses both of the hypotensive and of the hypertensive eye (fig. 6). This observation gives evidence in support of the assumption that the characteristic disproportion in the phases of the light reflex cannot be due to the hypertension alone. In this case, however, the speed of the primary phase of contraction of the hypotensive eye seemed somewhat diminished (4.3 mm. per second). According to our observation, this may have been caused by damage of the muscle of the iris; this damage may have been due to the hypertension, which existed before the operation or, directly, to the same factor that caused the hypertension, or, lastly, it may have been the expression of modifications in the tonus of the sympathetic nervous system.

The explanation of our observations becomes possible in the light of the facts we mentioned earlier in the paper, and previously discussed in

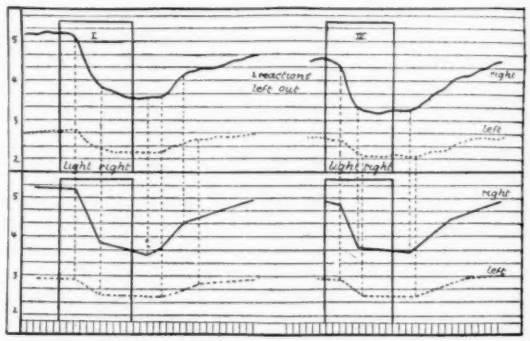

Fig. 6.—Bilateral simple glaucoma in a man aged 49. After previous cyclodialysis on both eyes, the right eye was hypotensive and the left eye hypertensive.

First line: First and fourth reactions of the right pupil to light, the left pupil reacting consensually.

Second line: Scheme of the reactions, showing the phases of contraction and redilation.

First reaction to light: The secondary and tertiary phases of contraction are undistinguishable. The ratio of the primary phase and the secondary and tertiary phases is 4:1.

Fourth reaction: The secondary and tertiary phases of contraction are absent, while the primary phase is practically unchanged (about 1.2 mm.). The consensually reacting left pupil shows only a primary phase of contraction, since the secondary and tertiary phases are completely absent. The primary phase of contraction is inextensive and sluggish.

detail,[2b] namely, that the absence of the secondary and tertiary phases of contraction depends on disturbances in the sympathetic innervation and, furthermore, that a certain functional tonus of the sympathetic system is required to guarantee a maximal parasympathetic reaction.

On the other hand, the cases described here are, indeed, not characterized by simple absence

of sympathetic innervation, since the psychosensory dilation reflex was present, sometimes even in its full extent (fig. 7). In all these cases, however, another phenomenon, which generally is considered predominantly of central sympathetic origin, was either poorly developed or absent, namely, the psychosensory restitution phenomenon (fig. 7). This dissociation between psychosensory dilation (which remained) and the psychosensory restitution phenomenon (which was absent) suggests the conclusion that the damage should be sought not in the peripheral sympathetic pathways but in or above the central inhibitory sympathetic pathways passing to the parasympathetic nuclei. This assumption is in accordance with the fact that glaucoma could never be produced experimentally by simple section of the peripheral sympathetic pathways. Since the number of cases in which pupillographic examination has been made is relatively small, one can only state that glaucoma creates

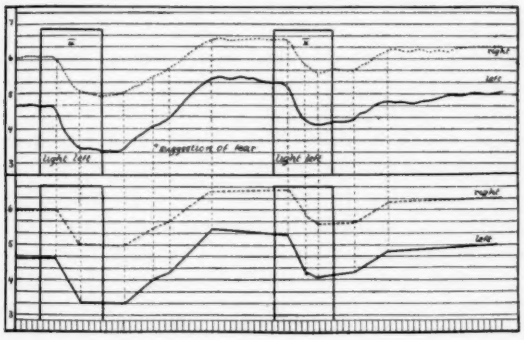

Fig. 7.—Unilateral simple glaucoma of the left eye.

First line: Fourth and fifth reactions to light of the left pupil. Between the fourth and the fifth light stimulus a psychologic stimulus was interposed, which produced a good psychosensory dilation. The psychosensory restitution phenomenon, however, was poor.

Second line: Scheme of the reactions, showing the phases of contraction and dilation.

Fourth reaction: Absence of the secondary and tertiary phases of contraction.

Fifth reaction: Traces of a secondary phase of contraction reappear; however, the reaction soon changes to dilation. The primary phase of contraction remains sluggish and is not intensified, as compared with the first reaction.

pupillary disturbances which are primarily of central nervous origin; they are based particularly on lesions of those centers which take part in the sympathetic innervation of the pupil. At a very early stage, in which symptoms of glaucoma are not yet present or are slight, the pupillary reaction to light shows increased fatigability; this fatigability shows, as far as the phases of contraction are concerned, characteristics of the type one finds associated with weakening of sympathetic factors. At a more advanced stage the contraction to light is of the same type as that in cases in which the central sympathetic factors, normally effective in the phase of contraction, are completely absent.

This does not mean, of course, that pupillary disturbances are responsible for the development of primary simple glaucoma. But it does indicate that they are regularly associated with simple glaucoma. They frequently precede ocular hypertension and, as in the case of the supposedly unaffected eye of unilateral glaucoma, indicate lesions in the centers and pathways of pupillary control, as well as peripheral lesions in the receptor and effector organs. This means, possibly, that intraocular hypertension, pupillary disturbances, damage to effector organs, retinal lesions and the like constitute a syndrome in which all symptoms, intraocular hypertension included, are to be considered as equivalent expressions of the same lesion of the central nervous system. Within this syndrome, each symptom may be more or less developed, or even nonexistent, i. e., clinically not ascertainable.

According to the observations described here, it is certain that a central sympathetic factor plays a role in the genesis of primary simple glaucoma. It has not yet been shown, however, whether this central disturbance itself is primary, due, for instance, to a primary degenerative process in the central nervous system, or whether the degeneration itself is secondary to other etiologic factors, for example, nutritional deficiency or toxicosis. But it is certain that the lesion on which the syndrome depends lies within or above the inhibitory sympathetic pathways to the nucleus of the third nerve.

SUMMARY AND CONCLUSIONS

In all the cases of primary simple glaucoma studied, constant characteristics of the pupillary reflex to light were shown by both eyes.

In all the cases of the initial stage of the disease, the pathologic feature in the reflex to light was a disproportion between the primary phase of contraction, on the one hand, and the secondary and tertiary phases, on the other, the former being more or less preserved and the latter being decreased or absent. This disproportion is known to be due to a central sympathetic condition.

In all cases of advanced simple glaucoma, and frequently in cases of the initial stage as well, additional modifications were detected; the primary phase of contraction was sluggish and less extensive and was preceded by a longer latency period.

In cases of unilateral simple glaucoma the clinically unaffected eye showed pupillographic features characteristic of simple glaucoma. In some of the cases the pupillary disturbances were of purely central sympathetic origin; in others the sympathetic type was modified by ocular factors.

The occurrence of characteristic pupillary disturbances in the clinically unaffected eye points to the presence of latent glaucoma in that eye. This assumption involves the supposition that demonstrable increased intraocular pressure is preceded by centrally conditioned pupillary disturbances.

Intraocular hypertension is only one symptom in a syndrome in which ocular hypertension, lesions of the receptor and effector organs within the eye, and so on, exist as equivalent expressions of the same central lesion. Each symptom may be more or less developed, or even clinically unascertainable. This is true for intraocular hypertension (for instance, the latent glaucoma of the clinically unaffected eye in cases of supposedly unilateral glaucoma), as well as for other symptoms.

Although lesions of the central nervous system appear to be an important factor in the genesis of simple glaucoma, it is not certain whether such lesions, although organic, are primary or secondary to other etiologic factors, such as nutritional deficiency and toxicosis.

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DISCUSSION

Dr. Mark Schoenberg, New York: Two years ago I approached Professor Lowenstein with the problem of making pupillographic records in cases of simple glaucoma. So far, over 40 cases have been studied by this method, and the information derived therefrom has proved to be most interesting and useful. The results of this investigation may be summarized as follows:

1. I became convinced that pupillography detects disturbances of pupillary reflexes which cannot be discovered by the naked eye.

2. In all our cases there appeared anomalies in pupillary reactions which seemed to be characteristic.

3. Experiments on animals and careful analysis of pupillographic curves in cases of simple glaucoma revealed that the hypothalamus or its connections to the midbrain are mainly responsible for the anomalous reactions of the pupils. The pupillary factor is to be considered as a component of the glaucoma syndrome, just as are the other components, such as ocular hypertension and progressive optic nerve atrophy, all of them depending, directly or indirectly, on the central lesion.

4. In cases of so-called unilateral glaucoma in which clinically there were no signs or symptoms whatever in one eye, the pupillographic method revealed disturbances in both eyes.

Since the pupillary reactions in the good eye may be disturbed long before the appearance of other signs or symptoms, we are led to conclude that a preclinical stage is present in simple glaucoma and that its diagnosis may be established by the pupillographic method.

This method enables one to make a diagnosis in an early stage and in doubtful cases of glaucoma simplex.

Pupillographic studies must be continued in a large number of cases of glaucoma and of other diseases in order to clarify many questions connected with the problem.

Dr. E. D. Friedman, New York: All must pay a tribute of respect to Dr. Lowenstein for the industry and persistence with which he has followed this subject for the last twenty years, and for the great care with which he works. He and I have had a few chats on this subject, and I can perhaps offer him a bit of clinical confirmation of his thesis of the central origin of glaucoma. In 1923 I saw a patient, then aged 12 years, in Mount Sinai Hospital, and I followed her clinical course for twenty years, in the hope that some day I would have the opportunity to verify post mortem my clinical impression of the central origin of glaucoma. Unfortunately, however, the family did not cooperate. The patient had had bouts of fever and convulsions between the ages of 3 and 10 years, and at the time I saw her she also had external manifestations of dwarfism (stunted growth). Scleroderma-like changes were present in the skin of the lower extremities. The left eye was glaucomatous, with optic nerve atrophy, and five years later similar changes developed in the right eye. She presented oculomotor palsies first on the left side, and five years later on the right side. She also had periodic amenorrhea.

Later, there developed signs of involvement of the pyramidal tract (the Babinski sign and absence of the abdominal reflexes) on the left side, cerebellar symptoms and difficulty in upward gaze and in horizontal gaze to the left. All these signs and symptoms were interpreted as indicative of a lesion in the brain stem (the hypothalamic zone). The spinal fluid was normal. Roentgenographic examination revealed nothing significant except for bridging of the sella. The basal metabolic rate was — 15 per cent. Iridectomies had been done on both eyes, and she had only minimum residual vision.

I lost track of the patient for fifteen years, when I was informed that she had been admitted for oscillometric studies to the New York Post-

Graduate Hospital, service of Dr. Irving Wright. While she was there she had an episode of subarachnoid hemorrhage, from which she recovered. She returned home, where she died several months ago, evidently from another episode of subarachnoid hemorrhage. It was my belief in 1923 that possibly there was a disturbance in the central autonomic system, since the patient presented, along with signs of a lesion of the hypothalamus, involvement of the vasomotor system, scleroderma-like changes in the skin of the legs and glaucomatous changes in the eyes. I know that this is pure speculation, and I apologize for it, for I have no pathologic observations to corroborate my thesis; however, in view of Dr. Lowenstein's work and the fact that cerebral or psychic factors are known to exist in every case of glaucoma, I do not think it is being too bold to say that glaucoma may really have a genesis in the central nervous system.

PUPILLARY REACTIONS OF THE SEEMINGLY UNAFFECTED EYE IN CLINICALLY UNILATERAL SIMPLE GLAUCOMA

PUPILLOGRAPHIC CONTRIBUTIONS TO DIAGNOSIS OF GLAUCOMA IN THE PRECLINICAL STAGE

OTTO LOWENSTEIN, M.D., AND MARK J. SCHOENBERG, M.D.
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The cause of simple glaucoma remains unknown. It cannot even be stated whether the primary cause should be sought within the eye itself or outside the eye, as in the nervous system, or in both.

A series of observations point to the probability that disturbances of the central nervous system are to be considered among the pathogenic factors of glaucoma. Thus it seems justifiable to take a stand on the question whether the disturbances of pupillary reaction, which so far have been present in all cases (about 40) of glaucoma studied, are of central origin or whether they originate in secondary modifications of the receptor or effector organs in the eye.

In this paper we present the results of pupillographic studies in which one eye was clinically unaffected. The question arises: How do the pupillary reflexes of the seemingly normal eye behave, and what is the significance of their behavior?

REPORT OF CASES [1]

CASE 1.—S. H., a man aged 43 (fig. 1), had a family history of both parents having suffered from diabetes mellitus for about ten years. The patient had scarlet fever at the age of 22, without any known after-effects; influenza, with a high fever but without loss of consciousness, at the age of 24, and herpes zoster in the same year. He recovered from the last two illnesses, without after-effects, in about one week. There was no history of syphilitic infection. He had been married for twelve years and had 1 child, 7 years old. He had had hypothyroidism since 1938. He was easily tired and had to continue taking thyroid. Neurologic examination (Dec. 30, 1941) revealed no pathologic condition.

He was first seen by one of us (M. J. S.) on Oct. 24, 1940. The patient reported that the symptoms of glaucoma began in May 1940, after a period of cumulative excitement. He had frequent attacks in which vision was blurred in the left eye and he saw rainbow-colored halos around lights. Occasionally he had pains in the left temple. The use of pilocarpine cleared up the attacks of blurring and of seeing halos.

Ophthalmologic Examination.—Vision was 20/20 in the right eye and 20/25 in the left eye. Inspection of the fundi revealed a normal appearance of the right optic disk and slight pallor of the left disk, with engorged veins.

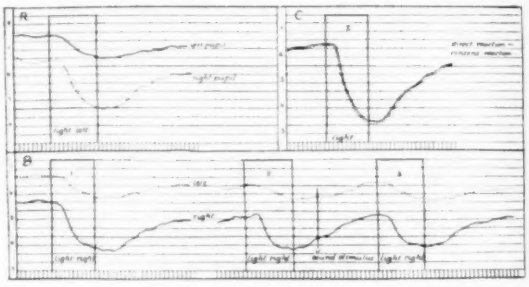

Fig. 1 (case 1).—Unilateral simple glaucoma of the left eye, in a man aged 43, the left pupil being larger than the right.

A, stimulation of the left pupil with light, the right pupil reacting indirectly.

B, stimulation of the right ("normal") pupil with light, the left pupil reacting indirectly. *I*, first reaction in a series of stimulations. The reaction is sluggish (as compared with that shown in *C*). *IV*, fourth reaction to light in the same series. The right pupil is excessively fatigable, with a latency period of about 0.4 second and a premature initial dilation preceding the contraction. *V*, fifth reaction to light in the same series. A sound stimulus is interposed between the fourth and the fifth reaction to light. The psychosensory restitution is poor. It is limited to restitution of the latency period, which appears shorter, while the initial dilation is no longer present. No deepening of the reaction itself occurs.

C, direct and consensual reactions to light of a normal subject (for comparison with *A* and *B*).

The intraocular pressure varied from 10 to 15 mm. of mercury in the right eye and from 10 to 15 mm. in the left eye as long as pilocarpine was used. After

This study was aided by grants from the Altman Foundation and the Oberlaender Trust.

Pupillographic Studies: VI. From the Departments of Neurology and Ophthalmology, New York University College of Medicine.

1. Recently one of us (M. J. S.) published a new classification of the stages of simple glaucoma. Four clinical stages were distinguished: (1) the functional, spontaneously reversible, stage; (2) the predominantly functional stage, with slight organic changes; (3) the predominantly organic stage, and (4) the completely organic stage. According to this classification, the disease in cases 1, 2 and 3 in this report was in the first stage, while the condition in cases 4, 5 and 6 was antecedent to the first stage, i. e., in the preclinical stage.

use of the miotic was discontinued for four days, the tension in the left eye was 28 mm. of mercury, and the eye became moderately congested.

Fields of Vision: There was slight disturbance at a tangent screen value of 1/1,000 mm.; repeated tests gave inconclusive evidence; the blindspots were enlarged.

Operation (April 1941).—An iridencleisis was performed on the left eye; recovery was uneventful.

Pupillographic Examination.—Inspection of the pupils revealed anisocoria, the diameter of the right pupil being 5.5 mm. and that of the left pupil 6.6 mm. The reaction of the left pupil to light was sluggish and less extensive than normal, with an extremely long latency period (more than 0.3 second). The contraction amounted to only 0.9 mm. The redilation, too, was sluggish. Psychosensory dilation and the psychosensory restitution of the left pupil were practically absent.

The pupillary response to light of the so-called normal (right) eye amounted to 1.9 mm. in the first reaction and to 1.2 mm. in the second and in the subsequent reactions. The right pupil was excessively fatigable. The latency period of the second reaction to light increased to about 0.4 second, and in the fourth reaction an initial dilation preceded the contraction (fatigue type). Both the psychosensory dilation and the psychosensory restitution phenomenon were poor. Both the contraction and the redilation showed pathologic features. While the reaction to darkness was almost absent on the left side, it appeared modified in its tertiary phase on the right side. The primary dilation was well developed.

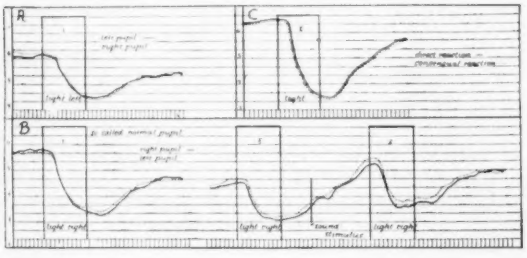

Fig. 2 (case 2).—Unilateral simple glaucoma of the left eye in a woman aged 59. The pupils were equal in size; however, slight anisocoria developed regularly after a certain number of stimulations with light.

A, reaction of the left pupil to light is slow; the latency period preceding contraction is increased, and the amount of contraction is only 1.6 mm.

B, pupillary reactions of the supposedly normal right eye. The contraction is slightly sluggish as compared with a normal one (*C*). Increased fatigability (fourth reaction) is characterized by a sluggish and small contraction after an increased latency period. Psychosensory dilation (after a sound stimulus interposed between the fourth and the fifth light stimulus) is well developed; psychosensory restitution, however, is poor. Note that the left pupil reacts better when stimulated indirectly than when stimulated directly. Slight dynamic anisocoria, however, is present after stimulation of the right pupil.

C, pupillary reflex to light in a normal subject (for comparison).

Case 2.—A. S., a woman aged 59 (fig. 2), had suffered from headaches for the past ten years but otherwise had never been sick. The menopause occurred at the age of 54. Neurologic examination showed no organic condition, but general nervous excitability was increased.

Ophthalmologic Examination.—Vision was 20/15 in the right eye and 20/20 in the left eye. Inspection of the fundi revealed pallor of the right optic disk and deep cupping and pallor of the left optic disk.

The anterior chamber of the right eye was normal, and that of the left eye was shallow.

Tonometric Examination: Pressure in the right eye was between 18 and 25 mm. of mercury without the use of a miotic. Pressure in the left eye was 35 mm. of mercury without a miotic and 18 to 25 mm. of mercury with a miotic.

Fields of Vision: The field of the right eye, as outlined on the tangent screen with a test object of 1 mm. at a distance of 1,000 mm. (1/1,000), remained good for

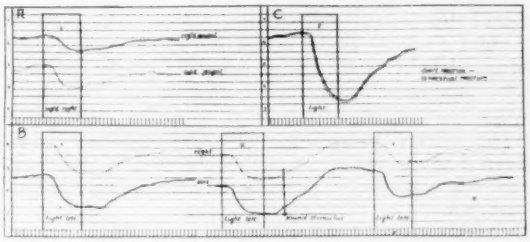

Fig. 3 (case 3).—Unilateral simple glaucoma of the right eye in a woman aged 46. The difference in the diameters of the pupils amounted to 1.6 mm.

A, reaction of the right pupil to light. Contraction, of no more than 0.6 mm., is preceded by a latency period of more than 0.4 second. The contraction is very sluggish. The consensual reaction of the left pupil is less sluggish and has a shorter latency period, but the contraction amounts to only 1 mm.

B, pupillary recation of the left, supposedly normal eye. The first contraction to light amounts to only about 1.6 mm. and decreases to less than 1.3 mm. in the following reactions. There is increased fatigability, and the latency period increases quickly to more than 0.3 second. Psychosensory dilation is well developed on both sides (after a sound stimulus interposed between the fourth and the fifth reaction to light), while psychosensory restitution is completely absent in both eyes.

C, pupillary reflex to light in a normal subject (for comparison).

two years. In the left eye the upper nasal field was defective. The patient had no complaints with respect to her right eye.

Both pupils were about 6 mm. in diameter. The left pupil reacted sluggishly to light, its contraction amounting to 1.6 mm. The latency period was increased. The redilation was slow. The psychosensory dilation and the psychosensory restitution phenomenon were present, although greatly diminished. The pupil of the right, or "normal," eye showed contraction to light of about 2.3 mm. While the type of contraction was fairly normal in the first reaction, it was quickly fatigable. The second reaction showed a latency period of more than 0.3 second, and the third reaction had an initial dilation. The psychosensory dilation was well developed. The psychosensory restitution phenomenon, however, was decreased. It is remarkable that the left pupil showed a contraction of 2.3 mm. in its indirect reaction but one of only 1.6 mm. in its direct reaction. The dilation to darkness was diminished on the left side and was normal on the right side. The secondary dilation, however,

was diminished on the right side also. In its indirect reaction, the right pupil reacted like the left pupil, and vice versa. The reaction to near vision was equal on the two sides.

CASE 3.—C. G., a woman aged 46 (fig. 3), came under our observation on Sept. 11, 1942.

She had been operated on for glaucoma in the right eye in December 1941. Twenty-four hours after the operation she had a sensation of paralysis of both upper and both lower extremities, lasting about five minutes. Since then, every morning on awakening, her eyelids seemed to be paralyzed for about forty seconds, so that it was temporarily impossible for her to open her eyes. Neurologic examination showed hyperactive patellar reflexes and diminution of vibration sense in the left leg. The neurologic diagnosis was "possible myasthenia pseudoparalytica gravis in its first phase."

Ophthalmologic Examination.—Vision was 20/20 in the right eye and 20/70 in the left eye. (The patient said her left eye had always been the poorer one.)

The anterior chambers were moderately shallow.

Inspection of the optic disks revealed optic nerve atrophy in the right eye, with deep excavation and engorged veins, and slight central cupping (physiologic) in the left eye, with pink color and slight engorgement of the veins.

Tension was 20 mm. of mercury (Schiøtz) in the right eye and 30 mm. of mercury (without use of a miotic for twenty-eight hours) in the left eye; with 2 per cent pilocarpine hydrochloride the pressure in the left eye became 25 mm. of mercury. This slight increase in tension without the use of a miotic was the only sign of glaucoma.

Fields of Vision: The upper half of the visual field of the right eye was contracted to 5 degrees from the fixation point. The left eye was normal.

Pupillographic Examination.—Inspection of the pupils revealed anisocoria, the diameter of the right pupil being 6.3 mm. and that of the left 4.7 mm. The right pupil showed contraction to light of 0.6 mm., after a latency period of more than 0.4 second. The redilation was slow. In its indirect reaction the right pupil contracted 1.2 mm., after a latency period of 0.3 second. Both the contraction and the redilation were less sluggish than those in the direct reaction.

In its first reaction the left pupil contracted to direct stimulation with light after a latency period of less than 0.3 second. The latency period, however, increased rapidly, while the contraction became sluggish. The contraction in the first reaction amounted to 1.6 mm. and that in the following reactions to less than 1.3 mm. The consensual reaction of the left pupil was more sluggish and less extensive than the direct reaction. The latency period for contraction was about 0.3 second in the first consensual reaction, and the extent of contraction was about 1 mm. Psychosensory dilation was well developed on both sides, particularly on the left. The psychosensory restitution phenomenon was practically absent bilaterally. The reaction to distant vision amounted to a dilation of 0.4 mm. on each side. While the reaction to darkness of the right pupil was diminished in its first phase of dilation on direct stimulation, it was present, although diminished, on indirect stimulation. On the other hand, the dilation to darkness was present in the left pupil on direct stimulation but was almost absent on indirect stimulation. The reaction to darkness of the left pupil was pathologic in its secondary dilation phase.

CASE 4.—H. F., a man aged 52 (fig. 4), was first seen by one of us (M. J. S.) on April 21, 1924, when his eyes were observed to be normal. He returned on May 18, 1942, complaining that for the past month he "could not focus" his right eye and that he had occasional pains around that eye. He saw rainbows around lights and had noted a line or streak across them for the past five days.

The diagnosis was noncongestive glaucoma of the right eye.

Ophthalmologic Examination.—The anterior chambers of the eyes were shallow, the depth being plus 3 in the right eye and plus 2 in the left eye.

The optic disks were of normal color; there was no cupping, and the veins were slightly engorged.

Vision was 20/15 in both eyes.

Visual Fields: The blindspot was moderately enlarged in the right eye and slightly enlarged in the left eye.

Tonometric Examination: The intraocular pressure measured 26 mm. of mercury in the right eye and 16 mm. with a 7.5 Gm. weight in the left eye. After one-half hour in the dark, tension was 30 mm. in the right eye and 15 mm. in the left eye. The tension of

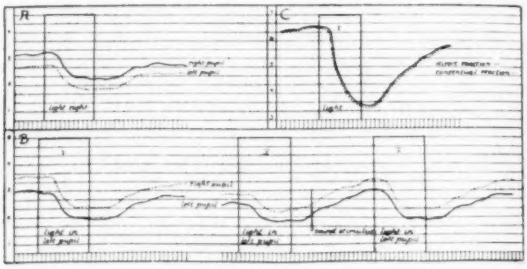

Fig. 4 (case 4).—Unilateral simple glaucoma of the right eye in a man aged 52. Anisocoria, with a difference of 0.5 mm. in the diameters of the pupils, was present.

A, reaction of the right pupil to light showing a long latency period (more than 0.3 second), followed by a sluggish contraction of only 1 mm. The indirect reaction of the left pupil is less sluggish.

B, reactions of the pupil of the left, supposedly normal, eye. An inextensive reaction of about 1 mm., following a latency period of more than 0.3 second, is rapidly exhausted. The fourth reaction is very sluggish, and the contraction amounts to 0.6 mm. The latency period for redilation after contraction is also prolonged. Psychosensory dilation (after a sound stimulus interposed between the fourth and the fifth reaction) is good on both sides. Psychosensory restitution (fifth reaction) is incomplete.

C, reaction to light in a normal subject (for comparison).

the right eye responded readily to administration of 2 per cent pilocarpine hydrochloride.

Neurologic Examination.—Slight differences appeared in the deep reflexes on the two sides, particularly in the patellar and triceps reflexes, which were exaggerated on the right side as compared with those on the left side. No symptoms of involvement of the pyramidal tract were noted, but muscle tone was increased on the left side. The Wassermann reaction was negative, and the personal history was noncontributory.

Pupillographic Examination.—Study of the pupils showed anisocoria, the diameter of the right pupil being 3.3 mm., and that of the left pupil 2.8 mm. The light reflex of the right pupil showed a long latency period

(more than 0.3 second). The contraction was sluggish and amounted to only 1 mm., and the redilation had a latency period of about 0.5 second. The indirect reaction of the right pupil was less sluggish, amounting to 1.15 mm. but having a latency period of 0.3 second.

The direct reaction of the pupil of the left, or so-called normal, eye was a little less sluggish than that of the right eye, but was rapidly exhausted, and its second reaction was deteriorated so as to show the same degree of sluggishness as did the first reaction of the right pupil. The latency period was more than 0.3 second. The indirect reaction of the pupil was more sluggish and less extensive than the direct reaction. The latency period for redilation after contraction to light was also prolonged to about 0.5 second.

Psychosensory dilation was good and psychosensory restitution was incomplete on each side. The reaction to near and to distant vision was equally disturbed on the two sides, as was the reaction to darkness.

CASE 5.—S. F., a man aged 50 (fig. 5), had had attacks of migraine since the age of 10 years; the pain was always on the left side, generally beginning in the late evening, before he went to sleep. In these attacks he was flushed and restless; the left side of his nose became congested, and he yawned frequently. After such an attack he was sick for a whole day. In 1930 he had the first attack of glaucoma, on the left side. There was no recurrence until ten years later, in 1940, when a similar attack occurred. The attacks had recurred every two to three months since.

Ophthalmologic Examination.—Vision was 20/20 in both eyes.

Examination of the fundi revealed no pallor or cupping of the optic disks.

The anterior chambers were shallow, the depth being plus 2 in both eyes.

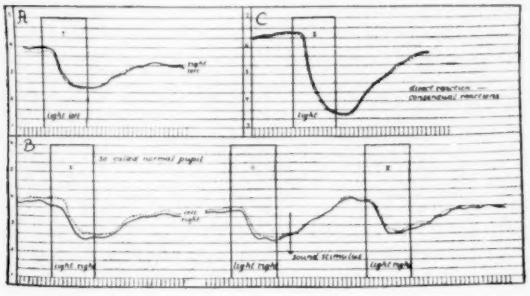

Fig. 5 (case 5).—Unilateral simple glaucoma of the left eye in a man aged 50, with unstable anisocoria, the maximal difference between the pupils being 0.3 mm.

A, reaction to light of the pupil of the left, or glaucomatous, eye. The contraction is sluggish and inextensive, amounting to 1.3 mm. The direct and the consensual reaction are identical.

B, pupillary reaction to light of the right, supposedly unaffected, eye. The reaction is at least as sluggish as that of the left eye and is rapidly exhausted, the fourth response showing a latency period of more than 0.3 second. Note the dissociation between the directly reacting right pupil and the indirectly reacting left pupil. Psychodilation (after a sound stimulus interposed between the fourth and fifth light stimuli) is good on both sides, and psychosensory restitution is poor (fifth reaction).

C, reaction to light in a normal subject (for comparison).

Tonometric Examination: The intraocular pressure varied from 20 to 17 mm. of mercury in the right eye and from 30 to 17 mm. in the left eye.

Visual Fields: Both blindspots were moderately enlarged.

Neurologic examination showed hyperactive deep reflexes, slight tremor of the fingers and a positive Romberg phenomenon, but no symptoms of true organic involvement of the nervous system.

The pupil of the left eye, 4 mm. in diameter, contracted after a latency period of 0.3 second. The contraction was sluggish and amounted to about 1.3 mm.

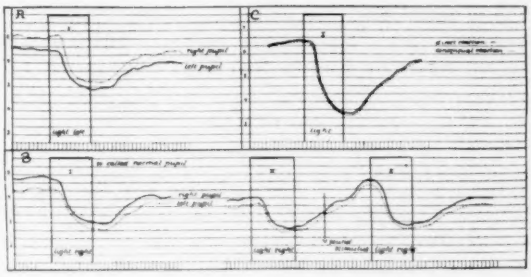

Fig. 6 (case 6).—Unilateral simple glaucoma of the left eye in a man aged 56. Anisocoria, with a difference in the pupils amounting to as much as 0.5 mm., exists.

A, pupillary reaction to light of the left, or glaucomatous, eye. The contraction is sluggish, amounting to not more than 1.6 mm., and is preceded by a latency period of more than 0.3 second.

B, reaction to light of the pupil of the right, supposedly unaffected, eye. The contraction in the first reaction to light amounts to about 2 mm. and fatigues rapidly, becoming more sluggish and decreasing to 1.3 mm. in the fourth reaction, while the latency period increases to more than 0.3 second. Psychosensory dilation (between the fourth and the fifth reaction to light) is well developed on both sides. The psychosensory restitution phenomenon, also, is comparatively well developed (fifth reaction); however, it disappears quickly. The pupillary contraction is followed by dilation while the light stimulus should still be effective—another symptom of poor restitution.

C, reaction to light in a normal subject (for comparison).

The reaction of the pupil of the right, so-called normal, eye was as sluggish as that of the left eye and was rapidly exhausted. Psychosensory dilation was good on both sides, and psychosensory restitution was poor. The reaction to near and to distant vision was good on both sides. The reaction to darkness was poor on both sides, particularly on the left side.

CASE 6.—S. D., a man aged 56, was first seen on Feb. 19, 1927, when he had no complaints or signs of glaucoma. Seven years later, in 1934, he first saw "rainbow-colored mists" around lights and had blurring of vision in the left eye. During the following years he had two to three attacks a year in the same eye.

Ophthalmologic Examination.—Vision was 20/30 in the right eye and 20/20 + in the left eye.

Examination of the fundi showed no cupping of the optic disks.

Tonometric Examination: The intraocular pressure was 20 mm. of mercury in the right eye and varied from 20 to 30 mm. of mercury in the left eye.

Visual Fields: The blindspot was moderately enlarged in both eyes, being somewhat larger in the right eye.

Pupillographic Studies.—There was slight anisocoria, the diameter of the left pupil being 4.7 mm. and that of the right pupil 5 mm. Contraction of the left pupil showed a long latency period of more than 0.3 second; it was sluggish and amounted to only 1.6 mm. The indirect reaction was better, the contraction being 1.7 mm.

The first direct contraction of the right pupil was approximately 2 mm., but the response rapidly became more sluggish and decreased to 1.3 mm. The psychosensory restitution phenomenon was comparatively well developed but disappeared quickly. Psychosensory dilation was well developed on both sides.

COMMENT

In these cases, and in others which we have studied but do not describe here, the pupillographic evidence indicates that pupillary disturbances limited to one side are not produced by simple glaucoma at all. Pupillary disturbances in simple glaucoma are always bilateral.

In most cases pupillary disturbances were more advanced in the glaucomatous eye than in the so-called normal eye. In no case, however, did the "normal" eye really show normal pupillary reactions. In several of our cases (3, 4 and 6) the pupillary reactions showed advanced disturbances on the so-called normal side, and in another (case 5) these disturbances were even more advanced than in the glaucomatous eye.

The question arises as to whether the pupillary disturbances allow one to draw any conclusions as to the location of the primary lesion which is responsible for them, either in the periphery (in the eye itself) or in the controlling organs of the nervous system.

Case 1 is particularly characteristic. The left pupil, i. e., the pupil of the affected eye, was larger than the right pupil. It contracted to light after a long latency period, and the reaction itself was sluggish and inextensive. The consensual reaction of the right pupil, however, was much less sluggish; its contraction was more extensive and more nearly normal, although it was still pathologic (fig. 1 *A*), as compared with a normal reaction (fig. 1 *C*).

The direct reaction of the right, supposedly normal, pupil (fig. 1 *B*) was also sluggish and inextensive as compared with a normal reaction (fig. 1 *C*). It fatigued quickly, as was readily shown by repeated stimulation with light; the fourth reaction showed all the symptoms of fatigue, i. e., a prolonged latency period, an initial dilation preceding contraction and a more sluggish contraction (fig. 1 *B*). The fatigued pupil, however, could be readily dilated by psychologic and sensory stimuli. The pathologically fatigued right pupil recovered (fig. 1 *B*, *V*) when a psychologic or sensory stimulus was interposed between the fourth and the fifth reaction. The fifth reaction was much better than the fourth, but did not yet show complete recovery, as is seen by comparison with the first reaction (fig. 1 *B*). These records demonstrate that the psychosensory restitution phenomenon was present in the supposedly normal eye, although to a decreased extent. The decrease in the psychosensory restitution was present, to a greater degree, in the diseased eye.

Can these modifications be explained by pathologic processes located within the eye? Such changes in the eye itself would be either in the light receptor organs of the retina or in the effector organs of the iris.

A. Damage to the Light Receptor Organs of the Retina.—When under the influence of a glaucomatous process, the cones of the retina are partly damaged; the original number of elements, therefore, is no longer able to receive the stimulus and to conduct it. A pupillary reflex is still present but is diminished. One can duplicate such a condition fairly well by decreasing the intensity of the light stimulus which is directed, centrally or paracentrally, into the eye. According to the "all or none" law, the effect of stimulation is the same as long as the same number of elements are stimulated, regardless of the intensity of the light stimulus. It is to be expected, however, that the number of stimulated receptors

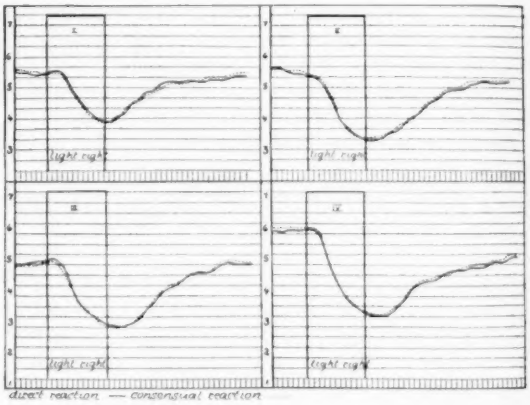

Fig. 7.—Varied pupillary reactions to light elicited by graded intensities of light stimuli in the same normal subject. The stimulus was always elicited by the same light source. The 100 watt, 6.5 volt bulb used was successively charged by 1 volt, 1.8 volts, 2.2 volts and 2.6 volts.

Reactions of different dimensions appear, the primary phase of contraction becoming longer the greater the intensity of the stimulus applied, while the secondary and tertiary phases remain identical.

The direct reactions are shown by solid lines; the indirect reactions, by dotted lines.

will decrease to the same degree to which the intensity of the stimulus is decreased; in this way, conditions become analogous to those in glaucoma in the event that the disease should have led to a partial destruction of the retinal receptors.

Figure 7 shows a series of experiments on the light reflex produced by each of a graded series of light stimuli in a normal subject. The applied light stimuli were always produced by the same light source, i. e., a 100 watt, 6.5 volt bulb successively charged by 1, 1.8, 2.2 and 2.6 volts.

It is evident that graded intensities of light stimuli elicit proportional variations in light reactions. It is also evident, however, that while the degree of contraction may be more or less decreased, the configuration of the light reflex remains the same regardless of the degree of light stimulation, that is, whether only a relatively small number of receptor elements are stimulated, or a greater number, or even all of them.

It is by these properties that the pupillary reaction of the normal eye is distinguished from that of the glaucomatous eye, which is not simply a normal reaction of diminished extent. This means that the modification of the configuration of the light reaction does not depend (at least, not exclusively) on possible modifications of the retinal receptors.

To this argument it could be objected that possibly an unequal distribution of the damaged elements exists in the glaucomatous eye, and that in the normal eye weak stimulation, when it was used, involved all elements of the fovea to the same degree. This objection, however, becomes invalid when weak stimuli are not directed into the eye centrally but come from a point in the periphery, so that chiefly the elements on the periphery of the retina are affected and the elements of the fovea are stimulated only weakly and irregularly, that is, to unequal degrees. In such experiments a modification of the reflex is not produced, but only a further diminution in the extent of the normal reflex of the pupil is effected.

B. Damage to the Iris.—It might be suggested that the pupillary changes associated with glaucoma are due to modifications in the iridal tissue. In that case, one must assume that the modification of the light reflex will be the same whether the eye is stimulated directly or indirectly.

Cases exist, it is true, in which both the glaucomatous eye and the supposedly healthy eye react equally poorly whether the stimulation is direct or indirect (figs. 1 and 6). In other cases of glaucoma, however, the same pupil differs in the degree to which it reacts, the extent depending on whether stimulation is direct or indirect (figs. 2 and 5). This means that the modifications of the pupillary reactions—both of the supposedly normal and of the glaucomatous eye—cannot be conditioned by damage to the iris. Therefore, one must assume the existence of two types of glaucoma, namely, one in which the iris is possibly involved and another in which the iris is certainly not involved.

In case 6 on stimulation of the glaucomatous eye with light, the consensual pupillary reaction of the supposedly healthy eye was better than the direct pupillary reaction of the diseased eye. This is evidence in support of the theory that in this case the receptors in the retina of the glaucomatous eye were not (or at least not solely) responsible for the pupillary disturbances. The direct pupillary reaction of the supposedly normal eye was poorer than the consensual pupillary reaction of the same eye—evidence that the condition of the iris certainly cannot be solely responsible, if at all. If the psychosensory dilation (the so-called ciliospinal dilation) is good in both pupils, it may be assumed that the dilator fibers of the muscle of the iris are not damaged. The psychosensory restitution phenomenon was incomplete on both sides with respect to the amount of the contraction, but was good with respect to the latency period and the speed of the contraction—evidence that the contraction fibers of the iris muscle cannot be seriously damaged, if at all.

Disturbances of the psychosensory restitution phenomenon are present on both sides in all cases, whether the pupillary damage is of lesser or of greater degree. This shows that if damage to the iris or the receptor elements is present at all, it must be, in any case, combined with central disturbances.

Case 4 was especially remarkable. The direct reaction of the right, or glaucomatous, eye was as extensive as the direct reaction of the supposedly normal eye. On the other hand, the pupil of the glaucomatous eye reacted better when stimulated indirectly, i. e., through the supposedly normal eye, than when stimulated directly. This might mislead one to the conclusion that disturbances of the receptors in the diseased eye were exclusively concerned. However, one is dealing not only with a diminished reaction, but with a pathologic modification of the reaction type, on both sides. Both pupils showed a good psychosensory dilation (ciliospinal reflex), an indication that at least the dilator fibers of the iris muscles were intact, and, since the pupils were very small (about 3 mm.) and contracted to less than 2 mm. it may also be assumed that the contraction fibers were intact. The psychosen-

sory restitution was poor (fig. 4 *B, V*), an indication that conditions of the central nervous system play a role.

All these facts and their evaluation suggest that, without recognizable rule, disturbances of retinal and iridal elements may occur in the supposedly normal eye which has not yet manifested glaucomatous disturbances clinically. They further suggest strongly that disturbances of the central nervous system play a role in all cases.

CONCLUSIONS

In all the cases of simple glaucoma studied pupillary disturbances accompanied the glaucomatous process, through all the stages examined, even the earliest. These pupillary disturbances proved to be bilateral; this was true even when clinically the glaucomatous process appeared to be unilateral.

Analysis of the pupillographic observations on the clinically unaffected eye in cases of unilateral glaucoma shows that a central nervous factor in the genesis of pupillary disturbances is always demonstrable.

While the central nervous factor is always present in the pupillary disturbances of the supposedly normal eye, functional modifications of either the retina or the optic nerve or both are frequently, but not always, present.

While we do not suppose that a causal connection exists between the pupillary disturbances and the glaucomatous process, we assume that both may be entirely or partially due to the same genetic factor, an assumption explaining the constancy with which pupillary disturbances accompany the glaucomatous process.

In view of (*a*) this constancy in the connection between pupillary disturbances and the glaucomatous process and (*b*) the fact that the clinically nonaffected eye in cases of unilateral glaucoma has so far shown pupillary disturbances, the pupillographic examination appears to promise a new way of establishing a diagnosis of glaucoma simplex in a preclinical stage.

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CAUSES OF IMPAIRED VISION IN RECENTLY INDUCTED SOLDIERS

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This report is the result of a survey undertaken to discover the causes of impaired vision in 10,532 of 190,012 recently inducted soldiers entering on basic training at Miami Beach, Fla. The survey was instituted at the suggestion and under the direction of Colonel Wilford F. Hall, Medical Corps, surgeon to the Station Hospital, Miami Beach Training Base. All the men were examined in the course of processing at the Eye Clinic of the station hospital. It should be understood that although the men came from all parts of the country, this study is not intended to represent a visual cross section of the eyes of American men between the ages of 18 and 36, as the induction boards had already eliminated enough of that group to make such a study impossible. Rather, the purpose of the investigation is to throw light on the pathologic reasons that the corrected vision of these men is below Army standards (20/40), usually in one eye, or sometimes in both eyes. In other words, if one excludes the men with correctible, purely refractive, errors, the report in the main is an ophthalmic classification of men placed in limited service because of their eyes.

The purpose of the visual processing was classification of the men for possible flying duty and for the various service schools maintained by the Army Air Forces Technical Training Command. When glasses were required, they were prescribed and ordered. In the processing, each man first had his visual acuity tested without glasses. Any glasses owned were then neutralized on the lensometer, and if vision with glasses was less than 20/40, the candidate was referred to the examining ophthalmologists and then subjected to refraction. In addition, men whose uncorrected vision was 20/40 or better, but not quite 20/20, received refraction in order that vision of 20/20 might be obtained for each eye and the inductee so qualify for certain types of flying duty.

Refraction for such large numbers of men made the routine employment of homatropine cycloplegia unfeasible, and its use was reserved for men with questionable vision, as well as for those who presented difficulties in examination of the fundus without mydriasis. A slit lamp was available, as were a perimeter and a tangent screen.

While the processing procedure was well planned and served its purpose of classifying large bodies of men with dispatch, and yet with considerable thoroughness, for the purposes of this survey several defects were noted in a review of the records. First, at times, especially during the early months of processing, no etiologic diagnosis was made. However, the only diagnoses significantly influenced by this policy were those of lesions of the macula (old central choroiditis) and corneal opacities. Sometimes, of course, an etiologic diagnosis was impossible. Perhaps the most important flaw in the survey was a tendency at the beginning, due to the unavoidable difficulties, to state merely in cases of amblyopia, that glasses did not improve a man's vision. As a result, a number of defects were classified as unexplained, rather than as refractive, amblyopia. The error thus introduced did not, however, alter any of the other categories and diminished as facilities were improved. One might estimate that under ideal circumstances probably not more than 5 per cent of the men recorded as having unexplained amblyopia would have been classified under refractive amblyopia. Organic diseases of the eye were ruled out in these subjects with amblyopia.

RESULTS OF STUDY

In 10,532 of the 190,012 men examined, it was found that vision in at least one eye could not be improved to 20/40. In table 1 are listed the main categories into which fell the ocular defects responsible for the visual impairment.

Amblyopia Due to Muscle Anomalies.—As noted in table 1, the amblyopia of a large number of men (24.22 per cent) was due to strabismus, either present or preexistent. This group represented 1.34 per cent of all the men examined. In addition to the usual classification, two types of lateral squint were differentiated: (1) squint with less than 10 degrees of arc, and (2) obvious squint.

Special care was taken in detection of small amounts of strabismus. If strabismus was not

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present, but the patient gave a history of squint, which often had been corrected by operation, and no other cause for the amblyopia could be found, his case was listed under a special heading but was included with the amblyopias due to muscle anomalies. Of the men with hypertropia, several presented complicated defects, and their cases were listed under spasm of the inferior oblique muscle (paresis of the superior rectus muscle), as this frequent anomaly was also present in these cases. Although patients with alternating strabismus were not included in the survey, as they did not have amblyopia, the cases of 101 men were noted, 73 of whom had alternating esotropia and 28 alternating exotropia.

TABLE 1.—*Causes of Poor Vision in 10,532 Men*

	Total Number of Men	Percentage of All Men Processed	Percentage of Men with Poor Vision
Amblyopia due to muscle anomalies	2,551	1.34	24.22
Injury	1,907	1.00	18.11
Inflammatory disease	195	0.10	1.85
Degenerative disease	107	0.06	1.02
Congenital anomalies	246	0.13	2.34
Refractive amblyopia	2,620	1.38	24.87
Unexplained amblyopia	2,509	1.32	23.82
Cause of pathologic condition unknown	397	0.21	3.77
Total	10,532	5.54	

In table 2 are summarized the data on the men with amblyopia due to muscle anomalies.

TABLE 2.—*Causes of Amblyopia in 2,551 Men with Muscle Anomalies*

	Number of Men	Percentage of Series
Esotropia (noticeable)	1,002	39.29
Exotropia (noticeable)	349	13.68
Esotropia (slight)	657	25.75
Exotropia (slight)	160	6.27
Hypertropia (spasm of inferior oblique muscle)	89	3.49
History of previous strabismus	294	11.52

Trauma.—The important role that injuries play in the causation of visual defects is well known, but the large number of patients observed in this survey, 1,907, with impairment of such origin came as something of a surprise. In other words, 1 per cent of all the men who came through the processing unit had lost useful vision in one eye as a result of an injury. Trauma was the cause in 18.11 per cent of the 10,532 men with poor vision.

In order to simplify tabulation, especially when several pathologic conditions existed in an eye as the result of a perforating injury, the cases of all men with defects due to this cause were placed under the heading of perforating injury. In other words, a patient might present an adherent leukoma, incarceration of the iris, traumatic cataract and detachment of the retina all in one eye, as a result of the injury, but the case was classified simply as one of perforating injury. Moreover, enucleation and phthisis of the eyeball following such injuries were made subheads. Perforating wounds caused 44.08 per cent of all injuries. When the injury, usually a contusion, caused damage chiefly to one structure, it was classified as injury of that structure, such as traumatic cataract or central chorioretinitis following a blow. Subtypes of traumatic cataract were aphakia following operation or spontaneous absorption of the lens. The high number of macular lesions following trauma is notable and might even be augmented by some of the cases of macular lesions listed as of unknown origin.

TABLE 3.—*Types of Lesions in 1,907 Men with Histories of Injury*

	No. of Men	Percentage of Series
Perforating injuries of eyeball	842	44.15
Enucleation following perforating injuries	438	22.97
Phthisis of eyeball following perforating injuries	49	2.57
Other conditions following perforating injury	355	18.61
Atrophy of eyeball following contusion	9	0.48
Injuries to cornea		
Corneal opacities	141	7.40
Birth injuries (tears in Descemet's membrane)	11	0.53
Injuries to iris		
Occlusion of pupil	2	0.11
Injuries to lens		
Traumatic cataract	541	28.38
Aphakia following extraction of cataract	125	6.55
Cataracts not operated on	416	21.29
Subluxation of lens	14	0.74
Injuries to vitreous		
Opacities and organization following hemorrhage	4	0.21
Injuries to choroid and retina		
Detachment of retina	53	2.78
Hole in macula, following solar retinitis	3	0.16
Central chorioretinitis	213	11.17
Rupture of choroid	17	0.89
Diffuse choroiditis	3	0.16
Injuries to optic nerve		
Optic nerve atrophy	51	2.68
Avulsion of optic nerve	3	0.16

Inflammatory Conditions.—Old inflammatory conditions did not play an important role as a cause of poor central vision. Only 195 men, or 1.85 per cent of the men with poor vision, had had an inflammatory disease. Probably the cases of a large proportion of the men with corneal opacities and central choroiditis recorded as of unknown cause belong under this head; even so, their inclusion would not alter the percentage significantly. Inflammations of the uveal tract, of course, make up the largest group, as is shown in table 4. Needless to say, except in 1, or possibly in 2, cases of active choroiditis, the condition was quiescent.

Degenerations.—As was to be expected, degenerative diseases played a small part in this survey—107 men were affected, or 1.02 per cent, of

those with a pathologic condition of the eyes. If 64 men with myopic degeneration had not been included, the role of degenerative processes would have been even less important. Moreover, in some of the 15 men listed as having macular degenerations the condition was probably of inflammatory origin, although in some it was definitely degenerative and bilateral. On the other hand, it is not unlikely that additional men with early keratoconus, of which 11 were discovered, had sufficiently good vision that they were not referred to the ophthalmologist in the processing line. The same held true for pigmentary degeneration of the retina, which was noted in 12 men. Corneal dystrophy, 3 instances of which were recorded, may have been overlooked in a similar way. Miliary aneurysms of the retinal vessels, a rare condition, originally desecribed by Leber, was seen in 2 candidates.

TABLE 4.—*Types of Inflammatory Lesions in 195 Men with Poor Vision*

	No. of Men	Percentage of Series
Opacities following corneal inflammation		
Nonspecific opacities	37	18.97
Trachomatous pannus	2	1.03
Interstitial keratitis	1	0.51
Iritis	6	3.09
Uveitis	19	9.74
Choroiditis (except central)	20	10.25
Central chorioretinitis	41	21.02
Complicated cataract	15	7.69
Optic neuritis	2	1.03
Primary optic nerve atrophy	40	20.51
Secondary optic nerve atrophy	8	4.10
Recurrent hemorrhage in vitreous (Eales's disease)	2	1.03
Retinitis proliferans	2	1.03

TABLE 5.—*Degenerative Conditions Noted in 107 Men with Poor Vision*

	No. of Men	Percentage of Series
Keratoconus	11	10.26
Corneal dystrophy	3	2,79
Epithelial 2		
Endothelial 1		
Pigmentary degeneration of retina	12	11.20
Macular degeneration	15	14.00
Myopic degeneration	64	59.90
Miliary aneurysms of retina	2	1.85

Congenital Conditions.—As was to be expected, a wealth of congenital abnormalities were encountered in the processing. Two hundred and forty-six men with such defects, or 2.34 per cent of all candidates with poor vision, were seen. By far the most common anomaly was cataract, which was noted in 126 candidates. Next in frequency was atypical coloboma of the macula, also known as fetal central choroiditis, which was present in 38 men; under this head the cases of some of the men with unclassified forms of central chorioretinitis undoubtedly belonged. A large number of men, 32, had typical colobomas of all forms, involving the iris, the lens and the choroid, and sometimes the optic nerve. Six men had had corneal opacities since birth. In 4 of these, and possibly in a fifth, the lesion was undoubtedly of congenital origin and occurred with anterior synechiae. Other anomalies included bilateral aniridia, congenital retinal fold, medullated nerve fibers involving the macular region and hypertelorism. Additional anomalies are listed in table 6.

TABLE 6.—*Congenital Lesions in 246 Men with Poor Vision*

	No. of Men	Percentage of Series
Microphthalmos	8	3.25
Microcornea	2	0.81
Corneal opacities	6	2.43
Corectopia	1	0.41
Aniridia (bilateral)	1	0.41
Atypical coloboma of the macula (fetal central choroiditis)	38	15.45
Cataract	126	51.22
Subluxation of lens	2	0.81
Defects in closure of the fetal fissure	32	13.01
Coloboma of iris, choroid and lens 5		
Coloboma of iris and choroid 14		
Coloboma of choroid 2		
Coloboma of optic nerve 2		
Coloboma of optic nerve and iris 1		
Coloboma of iris and lens 1		
Coloboma of iris 1		
Coloboma of choroid and optic nerve. 1		
Nystagmus	23	9.35
Medullated nerve fibers (extreme)	2	0.81
Persistent hyaloid artery	2	0.81
Partial aplasia of optic nerve	1	0.41
Pseudoglioma	1	0.41
Congenital fibrosis of lateral rectus muscle (Duane's syndrome)	1	0.41

TABLE 7.—*Refractive Amblyopia in 2,620 Men*

	No. of Men	Percentage of Series
Monocular refractive amblyopia	2,567	97.98
Binocular refractive amblyopia	53	2.02

Refractive Amblyopia.—Men with poor vision due to a high refractive error constituted the largest single group, numbering 2,620, or 24.87 per cent, of all those with a pathologic condition of the eyes. These candidates received generally more careful refraction than men with more easily correctible defects. Refractive amblyopia was present in one eye in 2,567 men and in both eyes in 53 men. As already mentioned, it is probalbe that some men with a condition recorded as amblyopia of unknown origin had refractive amblyopia.

Unexplained Amblyopia.—As was to be expected, men with amblyopia of unknown origin, with entirely normal ocular findings, formed an important group. A total of 2,509 men were encountered, or 23.82 per cent of all those with a

pathologic condition of the eyes. Of all the men processed, 1.32 per cent fell into this category. Monocular amblyopia was present in 2,495 men and binocular amblyopia in 14 men. In some of these men the condition was probably refractive amblyopia, but it is felt that few, if any, with organic disease of the eyes were placed in this group through error.

TABLE 8.—*Amblyopia of Unexplained Origin in 2,509 Men*

	No. of Men	Percentage of Series
Monocular amblyopia	2,495	99.44
Binocular amblyopia	14	0.56

Almost all of these men were checked carefully for possible malingering, and if any doubt existed as to the correctness of the results, the patient was returned for further study. Tests for malingering included the Wagner red, white and black chart, which requires only a red glass instead of the two color, red and green glasses usually used. As the patient's good eye is covered with the red glass and the supposedly poor eye is uncovered, there is less opportunity for him to cheat by closing it, unobserved. The mirror test, which doubles the distance of the letters from the patient, was of outstanding value, particularly in cases of binocular amblyopia. The value of routine confrontation tests should be particularly stressed; in both malingerers and persons with hysterical amblyopia these tests always revealed "tubular" fields, a pathognomonic sign. Relatively few malingerers or men with hysterical amblyopia were encountered in the processing. Instead, they were most frequently encountered on a return visit to the eye clinic for fancied ocular complaints, and detection was easier when there was a previous record of good vision. It is scientifically inaccurate, besides being unfair to the individual, to label a man as a malingerer, unless positive evidence is obtained: that is, the proving of normal vision by means of the special tests used. The tendency of examiners to classify a man as a malingerer merely because they can find no cause for the supposedly impaired vision is to be condemned except in rare instances.

Pathologic Conditions of Unknown Cause.—In this significant group are listed the men whose histories were too vague to permit an etiologic diagnosis and who presented a clinical picture which, likewise, did not indicate definitely the cause of the defect. This group included 397 men, or 3.77 per cent of all men with poor vision.

The most important condition encountered was old central chorioretinitis, which was noted in 263 men. In most instances the disease was probably inflammatory. In some men the condition was congenital, and probably in only a few was it of traumatic origin. Corneal opacities of unknown origin constituted another significant defect, being present in 128 men. Such lesions could probably be classified in the inflammatory or the traumatic category.

TABLE 9.—*Pathologic Lesions of Unknown Cause in 397 Men*

	No. of Men	Percentage of Series
Central (macular) chorioretinitis	263	66.25
Corneal opacity	128	32.25
Closure of central retinal artery	2	0.50
Old intraocular hemorrhage	2	0.50
Old retinal hemorrhage	1	0.25
Unclassified retinitis	1	0.25

Vascular accidents were also encountered, including closure of the central retinal artery in 2 men, old intraocular hemorrhage in 2 men and retinal hemorrhage in 1 man.

SUMMARY

Uncorrectible, impaired vision was encountered in 10,532 of 190,012 recently inducted soldiers.

Perhaps the most important result of the study was the observation that only one fourth of all men with poor vision had organic disease of the eye. In two thirds of the men with impaired vision of organic origin trauma was the etiologic factor, being usually the result of carelessness. In the case of the other three fourths it is possible that early care of the eyes might have prevented some of the resulting amblyopia, particularly the amblyopia resulting from strabismus and refractive amblyopia. When the condition was a pure amblyopia of unknown origin, it is less likely that early treatment would have been beneficial.

Thus, it seems fair to state that if proper attention had been given to the eyes of the 10,532 men studied, a significant percentage of the men might now be available for full, instead of limited, service. However, questioning revealed that with almost all the men with a neglected defect, especially those from large cities, where free care was readily available, the major factor was apathy, or even ignorance of the defect. Education, therefore, rather than the expansion of existing health facilities, appears to be needed.

CONJUNCTIVITIS AND KERATITIS OF ALLERGIC ORIGIN

ANALYSIS OF FIFTY-FOUR CASES

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According to O'Brien and Allen,[1] allergic dermatitis of the lids is not uncommon, but allergic keratoconjunctivitis is rare. Morrison[2] presented a verified case of allergic conjunctivitis and dermatitis resulting from the topical use of 5 per cent sodium sulfathiazole and 5 per cent sulfathiazole in a hydrous wool fat–petrolatum base. McAlpine and Berens[3] reported cases of blepharoconjunctivitis due to the use of tetracaine. Parlato[4] stated that allergy should be considered as an etiologic factor when chronic conjunctivitis, blepharitis and eczema of the lids have proved refractory to the usual treatment.

Balyeat and Bowen[5] classified allergic conjunctivitis as (*a*) the acute type, caused by animal dander, orris and eyelash cosmetics, and (*b*) the chronic type, divided in turn into the limbal and the palpebral form, caused by foods, pollens, animal dander, orris, dust and cosmetics.

Woods[6] discussed two steps in the diagnosis of responsible allergens—first, the taking of a history and, second, tests for the specific individual and group allergens. He expressed the belief that the best test is the intracutaneous injection of specific allergens.

The elimination of a certain element from local contact, from inhalation or from the diet with subsequent clearing of the lesion does not necessarily establish a diagnosis of allergy. In many cases in which allergic factors are suspected the observations on which a diagnosis is based are not conclusive. Patch tests, cutaneous tests for allergy and other necessary laboratory studies not only are difficult for the ophthalmologist to perform in the office but are somewhat out of his field.

In this series an attempt was made to select the patients in whose condition allergy was thought to be a definite factor. All but 5 of the patients were soldiers; all had primarily ophthalmologic complaints and were later referred to the allergist for a complete history with respect to allergy, a physical examination, cutaneous tests and an opinion.

History Analysis of Cases.—Twenty-three of the 54 patients, or 43 per cent, gave histories of allergy in the immediate family, while 10 in addition had close relatives with rather definite symptoms or diagnoses of allergic disease. Twenty had previous seasonal symptoms; these were worse in summer in 9 patients, in winter in 2 patients and in spring in 3 patients; the rest were troubled mostly in the fall. This observation may be compared with the results of Thomas and Warren,[7] who, in an analysis of 30 consecutive cases of allergic conjunctivitis, found that one third of their patients had a history of an allergic manifestation which had not been experienced in recent months. Eighteen of the present series of patients, or 33 per cent, gave indication in the history of previous allergic involvement of the eyes.

The recent change of environment which has accompanied the transfer of these soldiers from civilian to army life, in addition in many cases to a rather decided change of climate, may have had an influence on the present allergic condition.

Symptoms.—Lehrfeld[8] expressed the opinion that vernal conjunctivitis is a specific form of ocular allergy, and that if there is no itching, there is no vernal conjunctivitis. Twenty-five of the present series of patients had itching of the eyes or lids. Eighteen complained chiefly

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1. O'Brien, C. S., and Allen, J. H.: Allergic Keratoconjunctivitis, Arch. Ophth. **29**:600-604 (April) 1943.

2. Morrison, W. H.: Allergic Conjunctivitis and Dermatitis from the Topical Use of Sodium Sulfathiazole and Sulfathiazole, Am. J. Ophth. **25**:1104-1105 (Sept.) 1942.

3. McAlpine, P. T., and Berens, C.: Allergic Dermatitis (in Dentists) and Blepharoconjunctivitis Caused by Pontocaine, Am. J. Ophth. **25**:206-208 (Feb.) 1942.

4. Parlato, S. J.: Corneal Ulcers Due to a Common Allergen, Arch. Ophth. **14**:587-590 (Oct.) 1935.

5. Balyeat, R. M., and Bowen, R.: Allergic Conjunctivitis, South. M. J. **28**:1005-1011 (Nov.) 1935.

6. Woods, A. C.: Clinical Problem of Allergy in Relation to Conjunctivitis, Arch. Ophth. **17**:1-17 (Jan.) 1937.

7. Thomas, J. W., and Warren, W. A.: Analysis of Thirty Consecutive Cases of Allergic Conjunctivitis, Cleveland Clin. Quart. **7**:3-9 (Jan.) 1940.

8. Lehrfeld, L.: Vernal Conjunctivitis, Arch. Ophth. **8**:380-404 (Sept.) 1932; Eyelids and Conjunctiva as Shock Tissues in Allergy, Dis. Eye, Ear, Nose & Throat **1**:100-105 (April) 1941.

of watering of one or both eyes, and 18, of redness of the eyeballs. Fifteen said they had burning of the eyes, and 9 had as their chief complaint sore, itchy, swollen or irritated lids. Only 4 patients mentioned blurred vision.

Laboratory Data.—On examination, 35 of the patients were given Kahn tests of the blood, with negative results in all. One of the patients had previously had a positive Kahn reaction of the blood and at the time of examination was in the eighth month of antisyphilitic treatment.

TABLE 1.—*Types of and Reactions to Dust*

	Reaction			
	+	++	+++	++++
Dust, house	19	11	4	0
Dust, mattress	0	0	1	0
Dust, barracks	5	1	2	0
Dust, pine	1	5	0	0
Dust, warehouse and hospital	0	0	1	0
Dust, hospital	2	0	0	0

Teller,[9] in a study of 23 patients with vernal conjunctivitis, found that for more than 50 per cent the blood count revealed over 4 per cent eosinophils and almost all the patients had eosinophils in the conjunctival smear. Balyeat and Bowen [5] stated that smears usually show eosinophils.

Thirty-five patients in the present series had eosinophils in the blood, the average count being 2.9 per cent. The number of eosinophils varied from zero to 12 per cent. The patient with the 12 per cent count was referred to the gastroenterologist for clinical tests and examination of the stools in order to rule out the possibility that parasitic disease of the gastrointestinal tract was a causative factor. No evidence of parasitic disease could be obtained.

For 19 patients a differential count for eosinophils was made on smears of material from the conjunctiva, the average count being 4 per cent. The values varied from zero to 12 per cent. The absence of eosinophils in the smears of 11 patients brought the average to much lower than it would otherwise have been. For a patient with very acute keratoconjunctivitis the eosinophil count on the smear during the acute phase was 34 per cent. A similar count on a smear repeated at the end of one week, when the disease was in a more quiescent phase, revealed no eosinophils. The eosinophil count in general seemed to be much higher when the local reaction was more acute. No definite relation could be found between the eosinophil count of the blood and that of the smear, as the latter was likely to vary from day to day. Three of the patients for whom smears showed counts above 6 per cent had eosinophil counts of the blood averaging slightly over 4 per cent.

Five smears were taken from the conjunctiva, 3 of which showed no organisms and 2 gram-positive diplococci; 1 smear was negative for acid-fast bacilli. Of 14 cultures of material from the conjunctiva, 9 were sterile at the end of seventy-two hours; 3 showed Staphylococcus albus, with Staphylococcus albus haemolyticus in 1; 2 yielded Staphylococcus aureus, and 1, diphtheroid bacilli. It was thought that in these cultures the bacteria were either secondary invaders or contaminants.

Six patients had roentgenograms of the chest, and 7 had roentgenograms of the sinuses, with no significant evidence.

Data on Allergy.—Forty-nine patients had cutaneous tests against approximately ninety allergens, including bacteria. Of the patients not tested with the ninety allergens, 1 patient was tested with fifty-one allergens, 1 with thirty-three allergens and the rest with twenty allergens or less. The 3 women and several soldiers were given patch tests against suspected soaps or cosmetics.

As may be seen in tables 1 and 2, the results were classified as reactions to dust, the most common causative allergen, and reactions to the next ten most common allergens. It was felt that since dust itself and sensitivity to dusts are extremely prevalent, the reactions to such substances must be considered from a different standpoint than those to the other allergens. The sensitivity reactions to specific forms of dust are indicated in table 1. The results of tests for the common allergens are shown in table 2. In many cases in which sensitivity reactions of only 1 or 2 plus occurred, the ocular signs were the only physical indications of allergy. According

TABLE 2.—*Reactions to the Most Common Allergens*

Allergen	Reaction			
	+	++	+++	++++
Coffee	21	9	8	0
Feathers	13	16	3	1
Buckwheat	6	8	10	0
Tobacco	20	7	5	0
Banana	14	15	1	0
Barley	16	5	6	0
Wool	17	9	1	1
Cherry	30	4	1	0
Pyrethrum	15	9	2	0
Asparagus	12	6	5	0

9. Teller, I.: Allergic Investigations on Twenty-Three Cases of Vernal Conjunctivitis, Am. J. Ophth. **16**:149 (Feb.) 1933.

to Blank,[10] such a condition probably represents an ocular manifestation of allergy only, and the sensitivity would be demonstrated in other forms if the reaction were more pronounced.

Acute reactions (++++) were obtained for the following allergens in 1 patient each: sycamore, horse serum, corn meal, tomato, monilin, buckwheat, feathers, wool and rabbit. Two patients showed 4 plus reactions to trichophytin. It is interesting to note that in only 2 patients who gave 4 plus reactions was the allergen one of the ten most common allergens.

Woods[6] stated that it is important to make local ophthalmic tests with a 1:10 or a 1:100 dilution of the strength used for cutaneous tests when there is doubt as to the specific allergen. Ophthalmic tests were made on only 1 patient in this series.

Physical examination for allergy revealed asthma in 7 patients and allergic rhinitis in 10 patients, as well as ocular signs of allergy, such as allergic dermatitis of the lids (4 patients), scars of old keratitis of possible allergic origin (2 patients) and chronic vernal conjunctivitis (3 patients).

Physical Signs.—The conjunctival and corneal signs varied with the acute, chronic and recurrent types of allergic involvement. In the acute form of allergic conjunctivitis, the conjunctiva was moderately injected and slightly edematous, particularly on the palpebral surfaces, the process being more conspicuous in the lower cul-de-sac. Balyeat and Bowen[5] observed uniform injection of the conjunctiva, occasionally localized, with the acute type. This localized area of congestion, which was seen in several of our patients, simulated somewhat a phlyctenule on the bulbar conjunctiva and was comparable to an urticarial wheal of the skin. In 1 patient an area of edema extended into the cornea approximately 3.5 mm., the superficial half of the cornea being involved. Small or large follicles might or might not be present in the lower cul-de-sac. Their presence was not a diagnostic aid.

With the recurrent and chronic types, follicles were common, and both the upper and the lower palpebral surface of the conjunctiva were usually granular. The commonest feature of the chronic type was a velvety, boggy appearance of the palpebral surface, which was more pronounced in the lower cul-de-sac. Stringy mucoid discharge was usually present, in contrast to the watery discharge seen with the more acute type.

The classic cobblestone appearance of the conjunctival surface of the upper lid was presented by each of the 3 patients with vernal conjunctivitis.

It was surprising to find corneal involvement on examination with the slit lamp in many of the patients who seemed to have only conjunctivitis on gross inspection and examination with the loupe. Seventeen of the patients had gross corneal lesions. The majority of the early corneal lesions could be detected only with the slit lamp after the cornea was stained with a 1 per cent solution of fluorescein sodium. Small superficial stained areas were more noticeable on the surface 1 to 1.5 mm. from the limbal margin of the cornea on gross inspection and near the normal extensions of the vessels on examination with the slit lamp. As the condition progressed, these areas coalesced; infiltration became deeper, and discrete gross ulcers formed. The superficial vessels of the conjunctiva bordering on the lesion first became engorged, and later extended on to the cornea toward the infiltrated area (figure). Usually the infiltration and the surrounding edema increased in all directions, extended to the limbus and had a tendency to form an incomplete ring bordering on the limbal margin.

In several patients numerous gross erosions, with underlying infiltrations, were scattered throughout the cornea. During the acute phase of such a condition the vision of 1 patient was reduced temporarily to perception of hand movements at 2 feet (60 cm.). Balyeat and Bowen,[5] in several of their cases, described a vesicular eruption, discrete or confluent, at the border of the cornea.

Involvement of the central part of the cornea at first was never as severe as that at the periphery, but as the latter process increased in severity the central portion of the cornea began to show deep and superficial edema and occasionally breaking down, due to lack of nutrition. This was seen to a rather remarkable degree in a patient hospitalized for slightly over seven weeks.

Rankine,[11] in a report of 1,598 cases of keratitis due to artificial silk poisoning, described three stages: (*a*) edema or irregular swelling of the corneal epithelium and actual pinhead elevations of the epithelium, (*b*) desquamation and (*c*) rapid and complete repair. The healing of the corneas in the 17 patients with keratitis in the present series was not as rapid as that described by Rankine, and in several with more serious disease it seemed to be influenced directly

10. Blank, P., Maj., M.C., A.U.S.: Personal communication to the author.

11. Rankine, D.: Artificial Silk Keratitis, Brit. M. J. **2**:6-9 (July 4) 1936.

by the response to allergic desensitization. Vascularization from the conjunctiva was an important factor in the healing of ulcers near the limbus.

Differential Diagnosis.—The following conditions, with the characteristic features indicated, may be differentiated from acute allergic conjunctivitis:

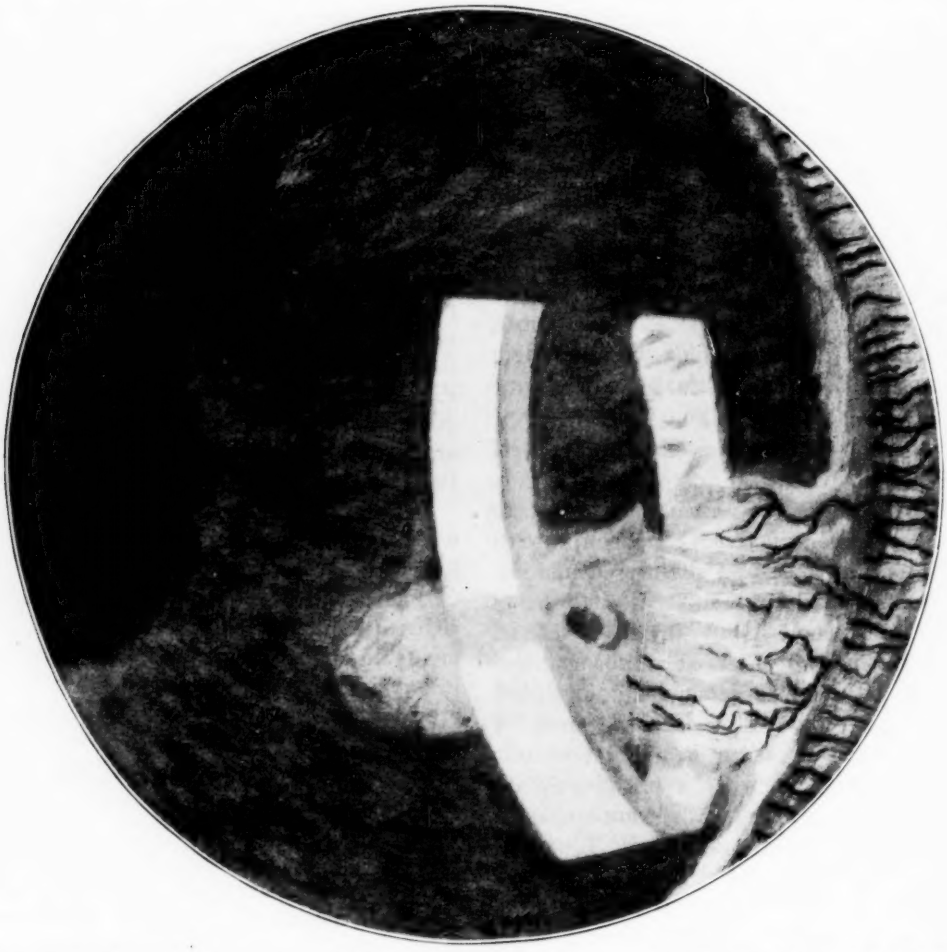
Acute Catarrhal Conjunctivitis: Usual presence of the causative organism in cultures and smears, more purulent exudate (as a rule) and frequent infection of the upper respiratory tract.

Acute Follicular Conjunctivitis of Beál: Rapid onset, complete resolution, presence of follicles, epidemic qualities and preauricular adenopathy.

Swimming Pool Conjunctivitis: Presence of many conjunctival follicles and of inclusion bodies, history of possible contact or epidemic and response to sulfonamide compounds administered locally and/or by mouth.

The following diseases, with the characteristics noted, can be differentiated from chronic allergic conjunctivitis:

Trachoma: Characteristic involvement of the upper lid, presence of Prowazek inclusion bodies, evidence on examination with the slit lamp of superficial pannus formation on the superior part of the cornea and, usually, a history of residence in the tropics or association with a trachomatous district.



Biomicroscopic view of the cornea and iris with a wide slit beam, showing the primary site of the allergic ulcer, with secondary extension of the infiltration toward the limbus, and corneal vascularization from the conjunctiva, an indication of early healing.

Parinaud's Syndrome: Sporothrix or Leptothrix in smears and cultures, and presence of preauricular adenopathy and chronic conjunctival granulations, which persist despite treatment.

Chronic Catarrhal Conjunctivitis: Presence of chronic infection of the tear sac, poor mechanical action of the lids, constant exposure to irritating chemicals or light rays, presence of dermatologic lesions on the lids or face, chronic involvement of the meibomian glands and possible

presence of the causative organisms in cultures or smears of material from the conjunctiva.

The following diseases, with the characteristics noted, can be differentiated from acute and chronic keratitis:

Bacterial Keratitis: Possible history of trauma, more frequent pain, frequent positive cultures of material from the cornea, more centrally located lesion, more pronounced conjunctival reaction and increased amount of edema surrounding the infiltration, apparent both grossly and on examination with the slit lamp.

Keratitis Rosacea: Presence of acne rosacea on the face, a rather characteristic tongue-shaped area of vascularization of the cornea, dilatation of the conjunctival vessels and, usually, good response to treatment with riboflavin.

Catarrhal Ulcers of the Cornea: Presence of primary acute catarrhal conjunctivitis, characteristic superficial ulcer formation on the limbal margin and a rather sharp healing response on treatment of the conjunctivitis.

Prognosis.—The prognosis, even for patients with severe keratitis, was always good. No secondary infections of the cornea occurred. Eight of the 17 patients with gross keratitis in this series required hospitalization. Six of these 8 patients had binocular and 2 monocular involvement. Only 5 eyes showed visual loss. The patient whose vision at one time, during the acute phase, was limited to ability to count fingers at 2 feet in one eye and was 4/200 in the other eye had a final visual acuity of 20/30 —2 and 20/25, two months after discharge from the hospital. The other 3 eyes showed less than 50 per cent loss of vision according to the Snellen chart, and 2 of these eyes had a loss of less than one third.

Although it was difficult to follow up and to evaluate the condition of these patients because of frequent Army transfers, recurrences were seen in 5 men. All, however, showed a much milder reaction at the time of recurrence than during the original attack. In 3 of these men the recurrence was of keratitis, and in 2, of chronic allergic conjunctivitis. All but 1 of these 5 patients had shown complete healing and relief from symptoms for two months before the recurrence. The patient whose condition never completely healed had recurrent corneal ulcers in one eye and presented evidence of sensitivity to bismuth and mapharsen; there was also a 2 plus reaction to barracks dust. Corneal involvement varied from gross ulcers 2 mm. in diameter to slight evidence of staining infiltration on examination with the slit lamp, but a lesion of some sort could always be noted at least once a month over a period of a year and a half. No pronounced symptoms were present after syphilitic treatment was discontinued (in the eighth month) and desensitization to dust begun.

Treatment.—Nearly every patient was observed for five to six days before being referred to the allergist. All men in whom keratitis was noted on gross examination were ordered hospitalized if there was no improvement in two days, as rigorous military duty could not be continued even though symptoms were not severe. On hospitalization, routine laboratory procedures were carried out, and the patient was referred to the allergist for cutaneous tests and statement of opinion.

On every patient desensitization was performed as a routine. Seven of the patients showed an acute flare-up of the disease at some time early in the desensitization treatment. In no case was the treatment discontinued during the flare-up, but the dose was diminished and then gradually increased to tolerance.

Three of the patients with keratitis and the 3 with vernal conjunctivitis could not be desensitized, owing to the great number of substances to which they were sensitive.

Local applications of 1:4,000 epinephrine hydrochloride with the addition of 10 grains (0.65 Gm.) of sodium biborate to the fluidounce (29.5 cc.) were given four times daily, preceded each time by use of cold compresses. These drops seemed to diminish the itching and the other symptoms present. For the patients with keratitis the usual treatment, with instillation of atropine, application of cold or warm compresses, administration of vitamin B complex hypodermically or by mouth, elimination of foci of infection and rest in bed if necessary, was followed routinely, and to 2 patients for whom desensitization failed intramuscular injections of milk were given.

CONCLUSIONS

A series of 37 patients with acute or chronic conjunctivitis and 17 patients with keratitis who had a suspected history and physical signs of allergy were referred to the allergist for cutaneous tests and desensitization. For all patients the prognosis was good, and it was believed that allergic desensitization produced improvement in all but 6, who presented sensitivity to various substances.

Major Philip Blank, Medical Corps, Army of the United States, performed the sensitivity tests on these patients, and my associate, Lieutenant Kenneth T. H. McFarland, Medical Corps, Army of the United States, made the drawing.

THE CORNEA

VI. PERMEABILITY CHARACTERISTICS OF THE EXCISED CORNEA

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While comprehensive investigations of corneal permeability have been few, numerous isolated observations, employing a variety of technics and test substances and leading to diverse conclusions, have been reported. The subject was reviewed in 1937 by Grönvall [1]; since this time 2 additional reports have appeared.[2]

Until recently there has been wide acceptance of Leber's thesis that the epithelium and endothelium were impermeable to water, since the corneal stroma did not appear to imbibe fluid from the tears or the aqueous. At the same time, these membranes have been thought to be permeable to various dissolved substances, notably, the drugs commonly used in ophthalmologic practice. In recent times, Fischer [3] claimed to have shown that the cornea possesses a unidirectional permeability, similar to that previously hypothesized by Wertheimer for frog skin. According to Fischer's interpretation, water, sodium chloride, oxygen, alkaloids and acid dyes pass through the cornea from without inward, while carbon dioxide, and probably basic dyes, penetrate in the opposite direction. Cogan and Kinsey,[2a] on the other hand, observed that the epithelium and endothelium of the excised cornea were practically impermeable to the passage of chlorides in either direction and were freely permeable to the passage of water in both directions. The corneal stroma was freely permeable both to chlorides and to water. These authors pointed out that this permeability was not only compatible with, but actually accounted for, the maintained deturgescent state of the corneal stroma. Swan and White [2b] measured the penetration of various substances into the cornea and found, in confirmation of Höber's observations on the amphibian kidney, that penetration did not take place by simple diffusion, so far as it did not vary with molecular size but, rather, occurred in inverse relation to the degree of polarity of the molecule.

It is our present purpose to report the permeability of the excised cornea to a series of test substances, with the aim of determining whether the barrier properties of the epithelium were (1) indiscriminate, that is, present for all substances which did not actually destroy the membrane; (2) dependent on charge, that is, different for anions, cations and nonelectrolytes; (3) dependent on molecular size, or (4) dependent on lipid-water solubility. Appropriate substances were selected on the basis of availability, the ease with which quantitative determinations could be made and the absence of toxic effects on the cornea.

The method employed for measuring the penetration of the cornea by various substances was essentially the same as that previously described for sodium chloride.[2a] Freshly excised beef corneas were tied onto the flared lower ends of graduated glass tubes. The tubes were partly filled with the test solutions and the lower ends immersed in a flask of suitable fluid. The amount of test substance which had penetrated from the tube into the flask was determined after an arbitrary period of eighteen hours. All experiments were run in triplicate at least. This was found to give sufficient information for classification of the substances according to their penetration of the cornea. It was not intended to obtain the mass of data that would be necessary for rigorous quantitative comparison of the individual substances.

The corneas were excised whole or after removal of the epithelium. As has previously been noted, this technic is suitable for study of the permeability only of the epithelium-stroma combination or of the stroma alone, since the endothelium is invariably removed by the manipulation and Descemet's membrane may be considered, with respect to its permeability characteristics,

From the Howe Laboratory of Ophthalmology, Harvard Medical School.

1. Grönvall, H.: Citric Acid Studies Referring to the Eye, Acta ophth., 1937, supp. 14, pp. 1-279.

2. (*a*) Cogan, D. G., and Kinsey, V. E.: The Cornea: I. Transfer of Water and Sodium Chloride by Osmosis and Diffusion Through the Excised Cornea, Arch. Ophth. **27**:466-476 (March) 1942. (*b*) Swan, K. C., and White, N. G.: Corneal Permeability: I. Factors Affecting Penetration of Drugs into the Cornea, Am. J. Ophth. **25**:1043-1058, 1942.

3. Fischer, F. P.: Untersuchungen über Quellungsvorgänge und über Permeabilitätsverhältnisse der Hornhaut, Arch. f. Augenh. **98**:41, 1928; Ueber die Permeabilität der Hornhaut und über Vitalfärbungen des vorderen Bulbusabschnittes mit Bemerkungen über die Vitalfärbung des Plexus chorioideus, ibid. **100-101**: 480, 1929.

as a part of the stroma. The cornea was tied on the tube with the epithelial, or outer, side of the cornea toward the lumen. The transfer of test substance, unless otherwise indicated, was in the direction anterior to the posterior surface of the cornea. The area of the cornea exposed to the lumen of the tube was approximately 0.4 sq. cm.

One cubic centimeter of the test solution was placed in the tube. The concentration used differed for the various test substances. The solutions were not stirred during the test period. The fluid in the tube was hypertonic to that in the flask by at least 0.2 mol of sodium chloride, or its osmotic equivalent. Sodium chloride was added to the test solutions when necessary to make the solutions hypertonic. All solutions had a hydrogen ion concentration of approximately p_H 7.

Water was used as the fluid in the flasks in all experiments except those involving purely fat-soluble substances. Cyclohexane (hexamethylene) was used in experiments employing tributyrin, vitamin A and sudan IV, and purified kerosene, in the experiments involving carbon disulfide.

At the end of the eighteen hour test period the fluid in the flask was removed and analyzed for the amount of test substance which had been transferred. The results were corrected for blanks obtained from the experiments similarly conducted but without the test substance. When it was thought that considerable absorption or destruction of the test substance within the cornea might have taken place, the amount of test substance remaining in the tube after the experiment was also determined.

Finally, the cornea was checked for epithelial damage in instances in which the epithelium was supposed to be intact and, conversely, for the adequacy of the removal of epithelium in the instances in which the stroma only was being studied. This was checked either by testing the transfer of sodium chloride concomitantly with that of the test substance or by testing the transfer of fluorescein at the conclusion of the experiment. Normally, the epithelium is an effective barrier to sodium chloride and to fluorescein in 1.5 per cent solution of sodium chloride. When any appreciable amount of these substances was transferred under the aforedescribed experimental conditions, the epithelium was presumed to be damaged, and the results obtained with these substances were not included in the present series.

On the basis of their permeability through the cornea, the substances tested are readily classified. They characteristically fall into one of the following groups: (1) substances which pass through the stroma to a much greater degree than through the epithelium-stroma combination (table 1); (2) substances which pass through the stroma and the epithelium-stroma combination to not greatly different degrees (table 2), and (3) substances which do not pass through either the stroma or the epithelium-stroma combination (table 3). The data in these tables are self explanatory.

To determine whether or not the barrier properties of the epithelium-stroma combination were unidirectional, the permeability of the cornea was tested for passage in both directions of a number of the substances listed in table 1 by reversal of the corneal surfaces on the tube. The electrolytes so tested were chloride, bromide, iron (ferric ion), thiocyanate and phosphate, and the nonelectrolytes were urea, levulose and inulin. No difference in corneal permeability was found to transfer of substances in the two directions.

In the light of Michaelis'[4] observation that some membranes (apple skin, parchment paper and collodion) which showed an apparent impermeability to all ions dialyzed against water were permeable to cations dialyzed against a solution of sodium chloride, the permeability of the cornea to calcium (calcium chloride), to iron (ferric sulfate) and to bromide (sodium bromide) was measured, both water and solutions of sodium chloride being used in the flasks. The epithelium-stroma combination remained practically impermeable to cations and anions irrespective of the presence of sodium chloride in the flask. However, it was observed that in the absence of the epithelium less chloride was transferred in eighteen hours from tubes containing a molar solution of sodium chloride into flasks containing a molar solution of sodium nitrate than into flasks containing water (an amount equivalent to 30 mg. of sodium chloride in the former and to 50 mg. in the latter).[5]

For comparative purposes, the permeability of the conjunctiva and sclera was tested with some of the substances. The technic was similar to that employed in testing the permeability of the cornea. The sclera, with or without the conjunctiva, was tied onto the tube, with the conjunctival surface facing the lumen. In order to maintain the conjunctival-scleral relations as nearly normal as possible, the portions selected for study were those adjacent to the limbus. It should be noted, however, that the sclera of the beef eye is considerably thicker in this region than is the stroma of the cornea. The substances tested were chlorides, phosphates, levulose, alpha-naphthylamine, aniline, methylene blue (methylthionine chloride), hematoxylin, orange G, amaranth, orange I, light green SF yellowish, eosin and fluorescein. Somewhat less of the test substance was transferred through the sclera in eighteen hours than through the corneal stroma, owing to the greater thickness of the sclera,[6] while the amount transferred through the conjunctiva-sclera combination was somewhat greater than that transferred through the epithelium and stroma of the cornea. Nevertheless, the conjunctiva-sclera combination was a selective barrier to the same group of substances as was the epithelium-stroma combination of the cornea, albeit less effective.

In the corneal experiments listed in tables 1 and 2, water was transferred from the flask into the tube, as would be expected on the basis of osmosis, so long as the epithelium was present and acted as a barrier to the test substances. However, unlike the experiments in table 1, in which the amount of transfer was proportional to the degree of hypertonicity of the fluid in the tube, the substances listed in table 2 appeared partially to "block" the transfer of water through the epithelium. Thus, less water was transferred into the tubes which contained both test substance and solution of sodium

4. Michaelis, L.: Theory of Permeability of Membranes for Electrolytes, J. Gen. Physiol. **8**:33, 1925.

5. This difference was also observed in the transfer of chlorides from a molar solution of potassium chloride in the tubes, but not from a molar solution of calcium chloride, into flasks containing water and a molar solution of sodium nitrate.

6. When thinner portions of the sclera were used, such as sections from the posterior pole of the eye, there was no significant difference in the amount transferred.

TABLE 1.—*Substances Which Pass Through the Stroma to a Much Greater Degree Than Through the Epithelium-Stroma Combination*

Test Substance	Initial Concentration in Tube, Mg./Cc.	Per Cent of Total Transferred in 18 Hours: Epithelium and Stroma	Per Cent of Total Transferred in 18 Hours: Stroma Only	Analytic Test
Br⁻(NaBr)	15.0	1	70	Wuth, O.: J. A. M. A. **88**: 2013 (June 25) 1927
Cl⁻(NaCl)	15.0	0	70	Fajans, K.: Ztschr. f. phys. Chem. **97**: 478-502, 1921
Cl⁻(NaCl)	50.0	0	70	Fajans, K.: Ztschr. f. phys. Chem. **97**: 478-502, 1921
P(Na_2HPO_4 & KH_2PO_4 Buffer) *p*H 7	2.0	0.9	55	Fiske, C. H., and Subbarow, Y.: J. Biol. Chem. **66**: 375, 1925
SCN⁻(NaSCN)	13.7	1	93	Snell, F. D., and Snell, C. T.: Colorimetric Methods of Analysis, ed. 2, New York, D. Van Nostrand Company, Inc., 1936, vol. 1, p. 608
Fe^{++}($FeSO_4$)	50.0	<0.01	50	Snell and Snell, p. 300
Fe^{+++}($FeCl_3$)	50.0	<0.25	2	Snell and Snell, p. 300
Ca^{++}($CaCl_2$)	111.0	<1	25.3	Clark and Collip, in Todd, J. C., and Sanford, A. H.: Clinical Diagnosis by Laboratory Methods, ed. 8, Philadelphia, W. B. Saunders Company, 1935, p. 378
Glycerin	100.0	2	48	Colorimetric: Reduction of $K_2Cr_2O_7$
Levulose	70.0	2	36	Corcoran, A. C., and Page, I. H.: J. Biol. Chem. **127**: 601, 1939
Inulin	10.0	<0.2	8	Corcoran, A. C., and Page, I. H.: J. Biol. Chem. **127**: 601, 1939
Urea	3.1	1.6	36	Folin, O.: Laboratory Manual of Biological Chemistry, ed. 5, New York, D. Appleton-Century Company, Inc., 1934, p. 149
Methylene blue	0.1	0	ca 25	Colorimetric
Fluorescein	1.0	0	ca 50	Colorimetric
Hematoxylin	5.0	0	ca 63	Colorimetric
New fuchsin	Saturated solution	0	ca 7	Colorimetric
8-sulfonic naphthylamine	2.5	1.8	38	Bratton, A. C., and Marshall, E. K., Jr.: J. Biol. Chem. **128**: 537, 1939

TABLE 2.—*Substances Which Pass Through the Stroma and the Epithelium-Stroma Combination in Not Greatly Different Degrees*

Test Substance	Initial Concentration in Tube	Per Cent of Total Transferred in 18 Hours: Epithelium and Stroma	Per Cent of Total Transferred in 18 Hours: Stroma Only	Analytic Test
6, 8-sulfonic naphthylamine	2.5 mg./cc.	<0.5	2.3	Bratton, A. C., and Marshall, E. K., Jr.: J. Biol. Chem. **128**: 537, 1939
α-naphthylamine	1.7 mg./cc.	1.0	2.0	Bratton, A. C., and Marshall, E. K., Jr.: J. Biol. Chem. **128**: 537, 1939
Aniline	2.5 mg./cc.	30	60	Snell, F. D., and Snell, C. T.: Colorimetric Methods of Analysis, New York, D. Van Nostrand Company, Inc., 1936, vol. 2, p. 408
Glyceryl triacetate, 100%	100%	5	10	Colorimetric: Reduction of $K_2Cr_2O_7$
Glyceryl triacetate, 5%	5%	20	40	Colorimetric: Reduction of $K_2Cr_2O_7$
Alcohol (ethyl)	10%	35	50	Colorimetric: Reduction of $K_2Cr_2O_7$
Thiodiglycol, 100%	100%	3	10	Colorimetric: Reduction of $K_2Cr_2O_7$
Thiodiglycol, 5%	5%	8.5	53	Colorimetric: Reduction of $K_2Cr_2O_7$
Acetone	5%	10	34	Folin, O.: Laboratory Manual of Biological Chemistry, ed. 5, New York, D. Appleton-Century Company, Inc., 1934, p. 205

TABLE 3.—*Substances Which Do Not Pass Through Either the Stroma or the Epithelium-Stroma Combination*

Test Substance	Initial Concentration in Tube	Per Cent of Total Transferred in 18 Hours: Epithelium and Stroma	Per Cent of Total Transferred in 18 Hours: Stroma Only	Analytic Test
Serum protein	70 mg./cc. in water	0	0	Nephelometric
Congo red	0.5:100 in water	0	0	Colorimetric
Sudan IV	About 1 mg./cc. in cyclohexane	0	0	Colorimetric
Glyceryl tributyrate	10% in cyclohexane	0	0	Colorimetric: Reduction of potassium bichromate
Carbon disulfide, 5%	5% in kerosene	Damaged epithelium	0	Bell and Agruss: Indust. & Engin. Chem. **13**: 297, 1941
Vitamin A as halibut liver oil	740 U. S. P. units of vitamin A per cc. of halibut liver oil	0.5	0.5	Snell, F. D., and Snell, C. T.: Colorimetric Methods of Analysis, New York, D. Van Nostrand Company, Inc., 1936, vol. 2, p. 617

chloride than when equivalent concentrations of a solution of sodium chloride only were present. Indeed, in the presence of pure glyceryl triacetate and pure thiodiglycol, practically no water passed into the tube during the eighteen hours of the experiments so long as the epithelium was intact (0.07 cc. and 0 respectively), while considerable water was transferred into the tube when the epithelium was removed (0.14 and 0.23 cc. respectively). This blockage was reversible, since subsequent substitution for the test substance in the tube of the standard solution of sodium chloride showed that the corneas with intact epithelium possessed their normal degree of semipermeability. Our tentative explanation for this phenomenon is that the substances in table 2, being soluble in lipids, were absorbed into the epithelium [7] and formed a lipid barrier to the transfer of water. This does not occur in the absence of the epithelium.[8]

Since the cornea is permeable to some substances and not to others, several mechanisms of selectivity may be considered. In keeping with current theses of permeability, the cornea might be considered a membrane with sievelike properties determining the passage of substances by molecular size, or as a membrane with electrostatic properties permitting the passage of certain substances on the basis of charge or absence of charge, or, finally, as a membrane containing a solvent, or a series of solvents permitting the passage of such substances as possess the appropriate solubilities.

Obviously, corneal permeability cannot be accounted for solely by the pore theory, since the molecular sizes of the substances listed in table 2, which penetrate the epithelium-stroma combination, are considerably greater than those of many of the nonpenetrating substances listed in table 1. Nevertheless, penetration of various acid dyes through the isolated stroma appeared to be in the approximate order of the sizes of their particles (table 4).

As for the electrostatic hypothesis, it is true that electrolytes were uniformly retained by the epithelium, but so were many nonelectrolytes. Moreover, no exchange of ions occurred when different salts were present on each side of the cornea. Hence, charge or absence of charge cannot alone account for the differential permeability.

The one difference which is obvious in the substances of tables 1, 2 and 3 is their variation in solubilities. The test agents listed in table 1, which characteristically pass through the stroma but not the epithelium, are substances that are predominantly nonsoluble in fats.[9] The test agents listed in table 2, which pass through both the epithelium and the stroma, are substances that are characteristically soluble in both water and fat. The substances listed in table 3, which do not pass through the stroma or the epithelium-stroma combination, are substances that either have very large molecules (proteins and congo red) or are insoluble in water. Whether or not the test substances of table 3 penetrated the epithelium could not be determined with the present technic.

In consideration of the foregoing results, it is concluded that transfer through the cornea is largely a matter of phase solubility. Specifically, the epithelium is believed to be permeable to substances with a fat-soluble phase.[10] and the stroma to substances with a water-soluble phase. However, water itself is an exception, for it passes through the epithelium.[11] (While no comprehensive experiments have been conducted on the selectivity of endothelial permeability, the results of experiments in vivo with chlorides, on the one hand, and with atropine and aniline,[12] on the other, are consistent with the thesis that the endothelium has the same properties of perme-

TABLE 4.—*Permeability of the Corneal Stroma to Various Dyes, Related to Size of Particles* *

Test Substance	Approximate Percentage of Total Transferred Through Stroma in 18 Hr.†	Approximate Size of Particle ‡
Orange G	100	4.0 ± 0.4
Eosin	25	5.3 ± 0.5
Orange I	10	5.0 ± 0.3
Amaranth	10	6.1 ± 0.3
Light green S. F. yellowish	2.5	6.6 ± 0.4
Congo red	0	13.2 ± 0.8

* The initial concentration in the tubes was 5 mg. per cubic centimeter in all cases.

† None was transferred through the epithelium-stroma combination.

‡ From Gordon, H. K., and Chambers, R.: Particle Size of Acid Dyes and Their Diffusability into Living Cells, J. Cell. & Comp. Physiol. **17**: 97-108, 1941.

7. The fat content of the corneal epithelium is 10 per cent of its dry weight, as compared with 1 per cent of the dry weight of the stroma (Krause, A. C.: Biochemistry of the Eye, Johns Hopkins Press, 1934).

8. This result is consistent with the observations of Swan and White that some of the naphthylamines are taken up by the cornea most readily when the epithelium is present.

9. Glycerin is ordinarily considered to be soluble in lipids because of its solubility in the common organic solvents, but its solubility in fats, such as glyceryl trioleate and glyceryl tributyrate, is actually slight.

10. It is to be noted that the actual fat of the corneal epithelium which is responsible for the permeability properties is not known.

11. The paradox of water transfer through lipid membranes is what led Nathanson (J. Botan. **39**:607, 1904) to postulate his theory of mosaic distribution of the lipid elements on cell surfaces.

12. A report of this work is to be published subsequently.

ability as the epithelium.) For a substance to pass through the intact cornea it is essential, therefore, that it have biphasic solubilities.

The application of these observations to the practical matter of transfer of alkaloids through the intact cornea in vitro and in vivo will be discussed in a separate communication.

SUMMARY AND CONCLUSIONS

In a study of the permeability of the excised cornea to a variety of substances it was observed that purely water-soluble substances do not pass through the epithelium (nor, in all probability, through the endothelium), while purely fat-soluble substances do not pass through the stroma. With the exception of water, substances which do get through the whole cornea have characteristically biphasic solubilities. Transfer of substances across the excised cornea does not differ appreciably in the two directions. The conjunctiva has properties of permeability that are qualitatively similar to those of the corneal epithelium, but less rigorous, and the sclera has properties similar to those of the corneal stroma.

Howe Laboratory of Ophthalmology.

EXPERIMENTAL STUDIES OF OCULAR TUBERCULOSIS

VIII. A STUDY OF THE INCREASED RESISTANCE TO REINOCULATION AFTER RECOVERY FROM OCULAR TUBERCULOSIS SHOWN BY THE IMMUNE-ALLERGIC RABBIT

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In a previous study [1] it was noted that for an undetermined period after recovery from an attack of secondary ocular tuberculosis the previously diseased eyes were endowed with a relative immunity to reinoculation with tubercle bacilli. When such eyes were given an inoculation of tubercle bacilli which produced typical disease in the normal fellow eye, the recovered eyes showed only a transient reaction to the tuberculin in the inoculum and did not have a second attack of tuberculosis. The studies at that time indicated that this local resistance was not due either to an increase in the general systemic immunity or to an exhaustion of the reaction capacity of the eye. It appeared to be related to some local condition in the eye itself. The purpose of this paper is to report further studies on this phenomenon of increased local resistance.

These studies are reported in two parts. The first part consists of an experiment dealing with (1) the relation of vascularity to the apparent local increased resistance and (2) the duration of the apparent local increased resistance. The second part consists of a series of clinical and histologic observations concerned with the relation of the increased resistance to the presence of an active, though clinically unrecognized, focus of tuberculosis in the eyes.

EXPERIMENTAL STUDY

Studies already reported [1] showed that the lack of reaction to a second injection of tubercle bacilli was not due to a decrease in the general reaction capacity of such eyes. The recovered eyes showed pronounced reaction to tuberculin in the inoculum and reacted in characteristic manner to inoculation with Brucella organisms. The possibility that the apparent immunity was due to an exhaustion of the reaction capacity of the eyes was therefore dismissed. In the following experiment attention was centered on the possible relation of local increased vascularization to the local resistant state and on the duration of the apparent local immunity.

PLAN OF EXPERIMENT

The object of this experiment was to investigate the question: Is the vascularization resulting from the previous attack of ocular tuberculosis concerned in the increased resistance? To this end, in immune-allergic rabbits, a comparison was made of the reaction to inoculation in eyes with tuberculous vascularization and that in eyes with nontuberculous vascularization. To accomplish this, two groups of immune-allergic rabbits were prepared.

Group A: This was a group of immune-allergic rabbits which had recovered from an attack of ocular tuberculosis in one eye. These rabbits had been inoculated in the right eye with the usual dose of tubercle bacilli, and the resulting ocular disease had been allowed to run its course. At the beginning of the experiment these eyes were scarred and vascularized, but the disease had been clinically inactive for an average period of six weeks. A previous study [1] had shown that the resistance to reinoculation endured for at least this period.

Group B: This group consisted of immune-allergic rabbits with nontuberculous vascularization of one eye. They were prepared in the following manner: A series of immune-allergic rabbits were inoculated in the right eyes with either living Brucella organisms or Listerella monocytogenes. Since these organisms produced an irregular degree of vascularization, all the rabbits were given an additional intracorneal injection of killed staphylococci. The inflammatory symptoms and disease produced by these injections were allowed to subside. There resulted a clinically inactive condition, with conspicuous vascularization of the cornea and visibly dilated capillaries in the iris.

Group C: As controls, immune-allergic rabbits which had received no previous ocular injections were used. As additional controls, normal rabbits were inoculated in the eyes.

Before the test inoculations were made, specimen rabbits from groups A and B were killed and their eyes examined histologically to determine whether the degrees of vascularization in the eyes of the two groups were comparable. In general, the eyes of the rabbits in group B showed slightly more secondary vascularization than did the eyes of the rabbits in group A. In the rabbits in group B the inflammatory reaction had almost completely subsided, and there was little, if any, cellular infiltration.

Representatives of these three groups (A, B and C) and the normal controls were inoculated in both eyes

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

1. Woods, A. C., and Burky, E. L.: Experimental Studies of Ocular Tuberculosis: VI. The Effect of Sensitivity and Immunity on the Experimental Lesions of Ocular Tuberculosis, Arch. Ophth. **25**:62-74 (Jan.) 1941.

at two week intervals, from Nov. 22, 1940 until March 3, 1941. Each subgroup so inoculated consisted of 2 rabbits from group A (immune-allergic rabbits with clinically healed tuberculous uveitis in one eye), 3 rabbits from group B (immune-allergic rabbits with nontuberculous scarring and vascularization of one eye), 1 rabbit from group C (immune-allergic rabbits with normal eyes) and 1 normal rabbit. The inoculations were made in the anterior chamber with the usual dose of 0.25 cc. of the undiluted paper filtrate of a six week culture of the virulent human tubercle bacillus used in these experiments.

A comparison of the course and intensity of any resulting tuberculous disease in the various eyes inoculated permitted an estimate of the influence of the following factors: *A*. The effect of scarring and vascularization in themselves on the tuberculous lesion. This could be estimated by comparing any tuberculous disease in the right eyes of the rabbits in group A (tuberculous scarring and vascularization) with the tuberculous disease in the right eyes of the rabbits in group B (nontuberculous scarring and vascularization) and with the disease in the left eyes (previously normal) of these same rabbits. The course of the disease in the rabbits in group C (immune-allergic rabbits with previously normal eyes) acted as a control for these observations. *B*. The presence and duration of any increased local resistance in the recovered eyes. This was determined by the occurrence of any disease in the right (previously diseased) eyes and the left (previously normal) eyes of the rabbits in group A, the inoculated eyes of the rabbits in group C acting as controls. The reaction in the eyes of the normal rabbits acted as a further control for the activity and virulence of the inoculum. Since all these normal rabbits showed the usual reaction of delayed inflammation, with caseation and, usually, perforation, they will not be mentioned further.

The eight subgroups were inoculated in the manner described, at two week intervals. After inoculation each subgroup was kept under observation for a further period of sixteen weeks. The eyes of all rabbits were examined clinically each week, the degree of ciliary congestion, new vascularization and infiltration of the cornea, the presence of tubercles and inflammatory process in the iris and of cells in the aqueous and evidences of caseation and necrosis being recorded on a numerical scale. An estimate of the total activity in each individual eye was then made. These estimates were averaged and plotted on coordinate paper. The resulting curves showed the course of the disease followed by the various eyes over the period of observation. Thus, in figure 1 (which is shown as a specimen of the curves for each subgroup), curve *A* represents the course of the tuberculous disease in the formerly tuberculous right eyes of the rabbits in group A; curve A^1, the average course of the disease in the previously undiseased left eyes of the rabbits in group A; curve *B*, the average course in the nontuberculous vascularized and scarred right eyes of the rabbits in group B and curve B^1, the course in the previously normal left eyes of the same rabbits. Curve *C* represents the average course of the disease in both the right and the left eye of the rabbits in group C, and curve *D*, the average course in the right and the left eye of the normal control rabbits.

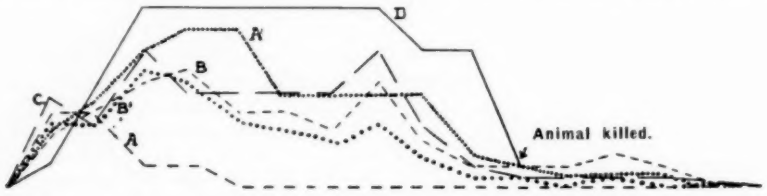

Fig. 1.—Course of tuberculous ocular disease in specimen subgroups of rabbits.

Curve *A* represents the sensitivity of the right eye (tuberculous vascularization) of rabbits in group A; curve A^1, that of the left eye (previously normal) of rabbits in group A; curve *B*, that of the right eye (nontuberculous vascularization) of rabbits in group B; curve B^1, that of the left eye (previously normal) of rabbits in group B; curve *C*, that of both eyes (previously normal) of immune-allergic control rabbits, and curve *D*, that of eyes of normal control rabbits.

EXPERIMENTAL RESULTS

1. *Relation of Local Vascularization to Local Resistance.*—The increased vascularization in the eyes of the immune-allergic rabbits in group B did not result in any increased resistance to subsequent inoculation with tubercle bacilli in any of the eight subgroups. In all the nontuberculous vascularized right eyes and the previously normal left eyes of the immune-allergic rabbits of group B there developed a definite and typical ocular tuberculosis of similar intensity. In general, the severity of the tuberculous reactions in the rabbits in group B was slightly less than that shown by the control immune-allergic rabbits in group C. This difference, however, was within the range of variations shown by some other groups of immune-allergic rabbits. The degree of ocular tuberculosis resulting in the right eyes of the rabbits in group B was definitely greater than anything manifested by the rabbits in group A, in which the vascularization and scarring were the results of former ocular tuberculosis. It is clear, therefore, since more severe reactions developed in the highly vascularized eyes of the rabbits in group B than in the eyes of the rabbits in group A, that vascularization in itself was not responsible for the relative resistance to reinoculation shown by the rabbits in group A. Indeed, it appears quite possible that the increased vascularity of the eyes of the rabbits in group B may have predisposed them to an increased inflammatory reaction.

2. *Duration of Apparent Resistance to Reinoculation.*—In study VI [1] it was reported that for at least six weeks after apparent clinical recovery from an attack of ocular tuberculosis the recov-

ered eyes were resistant to the usual reinoculation. This was the maximum period of observation in this study. In the experiment just reported the period of observation varied from six to twenty weeks after apparent recovery, i. e., from the time the first subgroup was inoculated, on Nov. 22, 1940, until the last subgroup was inoculated, on March 3, 1941.

The right eyes of the rabbits of the first five subgroups of group A, inoculated every two weeks from Nov. 22, 1940 to Jan. 18, 1941, showed a definite resistance to reinoculation. After the local reaction to the tuberculin in the inoculum subsided, the right (previously diseased) eyes showed little further reaction, while in the previously normal left eyes there developed the usual ocular tuberculosis exhibited by other immune-allergic rabbits when similarly inoculated. This is shown in figure 2, which is a composite curve for the first five subgroups. In this figure, curve *A* represents the average for the reactions of the right (previously diseased) eyes of the rabbits in group A; curve *B*, the average course of the lesion in the previously undiseased eyes of the various other immune-allergic rabbits, and curve *C*, the average course of the disease in the normal control rabbits.

The right eyes of the rabbits in the last three subgroups in group A, inoculated February 3 and 17 and March 3, failed to show complete immunity to reinoculation. After the subsidence of the initial reaction to the tuberculin in the inoculum, there developed in the right eyes of the rabbits of these three subgroups a low grade, but clinically recognizable, ocular tuberculosis of gradually increasing severity. The resistance of

Fig. 2.—Composite chart for subgroups 1, 2, 3, 4 and 5. Curve *A* represents the average sensitivity to tuberculin of the right, tuberculous, eyes of group A rabbits; curve *B*, the average for the previously normal eyes of other immune-allergic rabbits, and curve *C*, the average for the normal eyes.

these eyes to reinoculation had diminished. Figure 3 shows the averages for the reactions in the last three subgroups. While the disease in these right eyes was less than in the controls, nevertheless, by the fifth week after inoculation of these eyes the tuberculous activity in the previously diseased eyes was nearly equal to that shown in the eyes of the other immune-allergic rabbits with no previous ocular tuberculosis.

The duration of the resistance to reinoculation was further tested by reinoculation of the eyes of immune-allergic rabbits in which the ocular disease had been inactive for one year. Study VII,[2] on the effect of desensitization on the ocular lesions, was terminated in May 1942. In May 1943, 32 rabbits survived from the experiment, and 14 of these were clinically free from any evidence of tuberculous inflammation in the eyes. The anterior chambers of both eyes of these 14 rabbits were then reinoculated. The reaction shown by the previously diseased right eyes and that shown by the previously normal left eyes of these rabbits were practically identical. In both eyes of all rabbits tuberculosis of about equal severity developed.

Fig. 3.—Composite chart for subgroups 6, 7 and 8. Curve *A* represents the average sensitivity to tuberculin of the right, tuberculous, eyes of group A rabbits; curve *B*, the average for previously normal eyes of other immune-allergic rabbits, and curve *C*, the average for the normal eyes.

It is evident, therefore, that resistance to reinoculation with tubercle bacilli manifested by eyes which have apparently recovered from an attack of tuberculosis, and which clinically appear inactive, is only transient. At best it lasts only about four months. After an interval of about this length, the eyes again become susceptible to reinoculation, and after a year there remains no vestige of any resistance to secondary reinoculation with tubercle bacilli.

CLINICAL AND HISTOLOGIC OBSERVATIONS

It was now clear that this transient resistance to reinoculation was not related (*a*) to a general immunity produced by the original systemic injection and enhanced by the secondary ocular injection (study VI), (*b*) to an exhaustion of the reaction capacity of the eye (study VI) or (*c*) to the increased vascularization resulting from the previous ocular disease. Therefore, to explore further the reason for this transient resistance to reinoculation, clinical analyses and histologic examinations were made.

In the interpretation of the results of inoculation experiments certain facts on the clinical course of experimental ocular tuberculosis should be kept clearly in mind. In this paper, and in previous papers of this series, the terms

2. Woods, A. C., and Burky, E. L.: Experimental Studies of Ocular Tuberculosis: VII. Effect of Desensitization with Tuberculin in Experimental Ocular Tuberculosis, Arch. Ophth. **29**:369-379 (March) 1943.

"healed" and "clinically inactive" have been used almost as synonyms. These terms carry the following implications: Such "healed," or "inactive," eyes showed no clinical evidence of active disease. The pericorneal congestion had subsided. The corneas, though scarred and often partially vascularized, showed no active infiltrates. The irises manifested no evidence either of actual tubercles or of active inflammation. The pupils were often occluded by organized exudates, so that ophthalmoscopic examination was impossible. When such examination was possible, although there was often clouding of the anterior portion of the vitreous, due to organization, there were no fresh vitreous veils, and the fundi, when visible, showed no exudates. The aqueous rays were negative.

TABLE 1.—*Data on Thirty-Two Rabbits One Year After Study on Effect of Desensitization on Ocular Tuberculosis*

Status of Eyes May 1942		No. of Eyes	Course 1942-1943: Inactive Disease	Course 1942-1943: Recurrence	Status of Eyes May 1943: Healed	Status of Eyes May 1943: Actively Diseased or Ruptured
Clinically inactive disease	A	11	7	4	7	4
	B	6	6	0	6	0
Trace of inflammation	A	3	3	0	3	0
	B	4	3	1	3	1
Active disease	A	0	0	0	0	0
	B	8	0	8	0	8

What was the subsequent fate of these eyes with clinically inactive and healed tuberculosis? A number of such eyes in rabbits, remaining from study VII,[2] on the effect of desensitization on the ocular lesion, were available for further study. At the end of this experiment, in May 1942, there remained 36 rabbits in the group which was treated with tuberculin (group A). In 1 of these rabbits the disease was still active; in 4 rabbits there was a trace of smouldering activity, and in 31 rabbits the disease was clinically inactive or healed. Of the untreated rabbits of the control group (B) there were 37 survivors. In 8 of these rabbits the disease was still active, in 4 rabbits there was a trace of activity, and in 25 rabbits the disease was inactive. During the year following the termination of study VII the mortality was heavy, and by May 1943 there were only 32 survivors, all told—14 in group A and 18 in group B. In 17 of these 32 survivors the disease had been clinically inactive in May 1942; 7 rabbits had shown a trace of inflammation, and 8 had had active inflammation at that time. The subsequent fate of these 32 rabbits is shown in table 1.

A study of this table reveals that of 17 eyes which were clinically healed, 4 had undergone recurrences and ruptured, while 13 showed no recurrences and still were clinically inactive one year later. Of the 7 eyes which had a trace of inflammation, 1 still had active disease one year later, while the condition in 6 had progressed to clinical inactivity or healing. All the 8 eyes which still showed activity in 1942 were those of rabbits in group B. In every rabbit the disease had progressed, and the eyes were virtually destroyed by tuberculosis one year later. The fate of the rabbits with a trace of inflammation was not remarkable. The results for the rabbits in these two categories were statistically the same for both group A and group B and require no comment. In summary, of the 14 survivors in group A, the eyes of 10 were healed, and those of 4 had ruptured. In group B, of 18 survivors, the eyes of 9 were healed and those of 9 had ruptured. Therefore, even though treatment with tuberculin had been discontinued with the rabbits of group A, the final results were better than those for the rabbits of group B. However, further analysis of the behavior of the rabbits which had clinically inactive disease in 1942 is possibly of significance.

There were 17 rabbits in this category—11 in group A, which had been desensitized, and 6 in group B, which had received no tuberculin and in which the apparent healing was spontaneous. Of the 11 desensitized rabbits, 4 had recurrences of the ocular inflammation, while the eyes of 7 remained healed. Of the 6 rabbits which had inactive disease and had received no tuberculin, none had recurrences. Thus, while the incidence of primary clinical healing was much greater in the desensitized group when the administration of tuberculin was stopped, there was a return of the sensitivity, and with this an incidence of recurrence of ocular tuberculosis of 36 per cent. On the other hand, in the group with spontaneous cessation of the tuberculous inflammation there were no recurrences. In support of the statement that sensitivity returned in these rabbits after tuberculin was stopped are the results of comparison of the sensitivity manifested by these animals in May 1942 with that shown in May 1943. The results of these determinations of cutaneous sensitivity are shown in table 2.

TABLE 2.—*Changes in Sensitivity to Tuberculin in Desensitized Rabbits During One Year*

	Cutaneous Sensitivity		Ocular Sensitivity: Right Eye Previously Desensitized		Ocular Sensitivity: Left Eye Previously Normal	
	May 1942	May 1943	May 1942	May 1943	May 1942	May 1943
Rabbits Desensitized (group A)	0.5 (—) (0.05 mg. P.P.D.)*	1.6 = (0.005 mg. P.P.D.)	0.36	0.6	0.27	0.6

* P.P.D. indicates purified protein derivative.

Thus in one year the cutaneous sensitivity increased from a reading of 0.5 to 0.05 mg. of purified protein derivative to that of 1.6 to 0.005 mg., three times the extent of the reaction to one-tenth the dose. The ocular sensitivity in the previously diseased right eye had increased from 0.36 to 0.6, and that in the normal left eye, from 0.27 to 0.6. This is in line with the well known clinical observation that after desensitization is accomplished by administration of tuberculin, the injections must be continued; otherwise sensitivity will almost invariably recur, with the danger of recurrence of the ocular inflammation.

However this may be, as a result of the observations thus far made on resistance and recurrence in experimental ocular tuberculosis, three facts become obvious: 1. The resistance of recovered eyes to reinoculation is not related to general immunity, to exhaustion of the reaction capacity of the eyes or to vascularization. 2. This resistance is transient. In eyes which showed no spontaneous recurrence (the only eyes thus tested), the resistance begins to fade in four months and is gone completely in one year. 3. Apparent clinical recovery is not an index of true healing—a large percentage of eyes which show apparent healing may manifest recurrent and violent tuberculous inflammation.

Fig. 4.—(*A*) Diffuse cellular infiltration of the ciliary body, and (*B*) inflammatory changes in the iris, in clinically "quiet" eyes (immune-allergic rabbits with secondary ocular tuberculosis).

The next point was to determine whether histologic study of these recovered eyes at various times after recovery or inoculation could throw any light on the question why some eyes were

resistant to reinoculation and some were not. To this end, eyes which had been clinically inactive for six weeks and were presumably susceptible to reinoculation were sectioned and studied. The salient observations were as follows: 1. Eyes sectioned six weeks after apparent clinical recovery still showed definite evidences of active tuberculous inflammation, with diffuse lymphocytic infiltration, epithelioid cells and macrophages, often with deep, usually well encapsulated, tubercles (fig. 4 *A* and *B*). 2. Eyes sectioned one year after apparent clinical recovery, during which there had been no recurrences, showed heavy, nonspecific scarring but no active cellular infiltration or tubercules, such as were present in recently recovered eyes.

This observation at once suggested that the increased resistance to reinoculation shown by recently recovered eyes might be due to the presence of an active, but clinically unrecognizable, focus, already present in the eyes—in short, to the premobilization of the factors of resistance, which had already controlled the original infection. Similarly, the susceptibility to reinoculation shown by eyes which had been clinically healed for a longer period might be due to the disappearance of these same factors of resistance—the macrophages and the epithelioid cells. Obviously, this proposition is not capable of absolute proof, for it is manifestly impossible to section an eye, demonstrate the presence or absence of active cellular infiltration and later reinoculate the same

Fig. 5.—(*A*) Iris and ciliary body, and (*B*) early tubercle on the iris, eleven days after reinoculation in an immune-allergic rabbit with old healed secondary ocular tuberculosis. × 160.

eye to determine its resistant state. Group inoculations, however, made this a plausible hypothesis—a group of apparently recovered eyes, specimens of which showed an active focus of tuberculosis with cellular infiltration, were resistant to reinoculation, while a group of eyes recovered for a longer period, specimens of which showed no active focus of tuberculosis and only slight cellular infiltration, were not resistant to reinoculation and a second attack of ocular tuberculosis developed on reinoculation with tubercle bacilli.

Further clinical and histologic examinations were made on 14 rabbits remaining from study VII [2] (immune-allergic rabbits with healed secondary ocular tuberculosis). This was done to determine whether these rabbits differed significantly from immune-allergic rabbits which had not undergone a previous attack of ocular tuberculosis with respect to the clinical course of a second attack of ocular tuberculosis and the histologic appearance of the eyes. These 14 rabbits were, therefore, reinoculated in the right eye, which had been the site of the former attack. Thereafter, at two week intervals after inoculation, sample pairs of animals were killed for histologic examination. Surviving rabbits were kept under constant clinical observation. These rabbits all showed a moderate initial reaction to the tuberculin in the inoculum. This usually faded within a week, and after a short latent period clinical symptoms of tuberculous

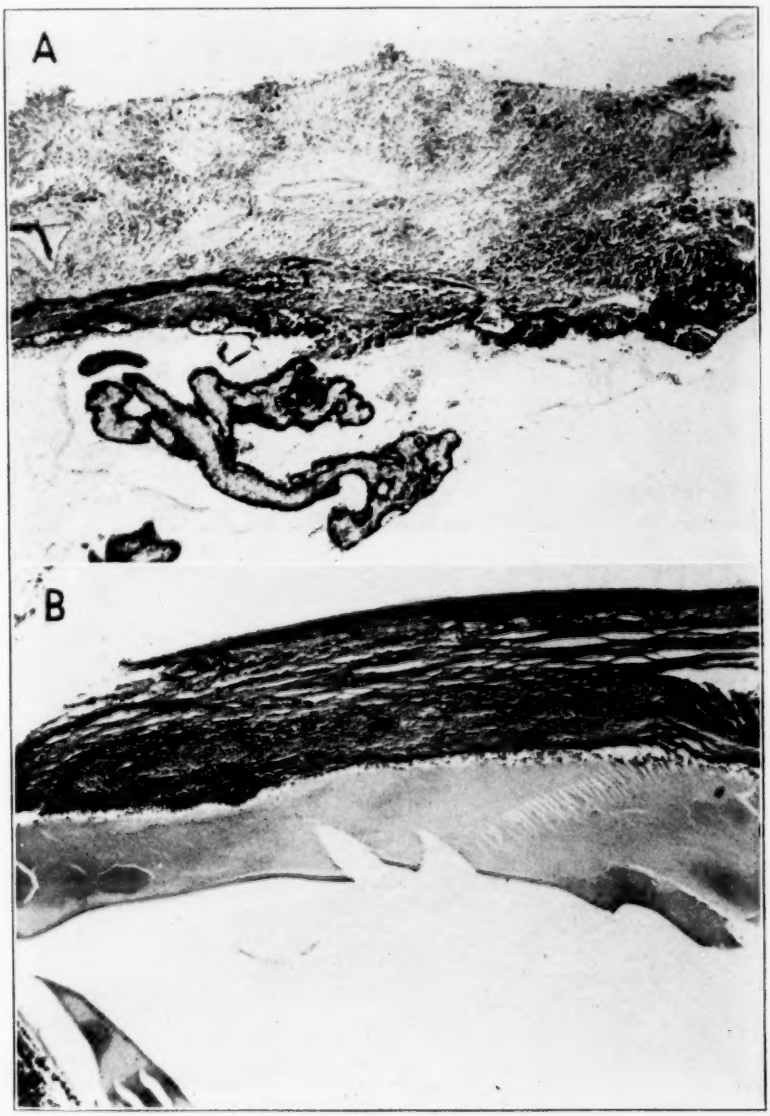

Fig. 6.—(*A*) Diffuse cellular infiltration of the iris, and (*B*) early tubercles of the cornea, nineteen days after reinoculation in immune-allergic rabbit with old healed secondary ocular tuberculosis. × 50.

inflammation developed. In the latter stages the disease tended to be more serious than is usually observed in immune-allergic rabbits, a few of the eyes showing caseation and necrosis and finally rupturing. In this respect the ocular disease simulated the picture observed in normal, non-immune rabbits and was possibly an index of the degree to which the immunity had declined in the individual animals.

The first rabbit employed for histologic study was killed eleven days after reinoculation of the eyes. In this rabbit the reaction to the tuberculin in the inoculum had been relatively moderate and had completely subsided. Histologic study of this eye showed old scarring of the iris and ciliary body and a minimum of cellular infiltration (fig. 5 *A*). The one evidence of early disease was a small tubercle forming on the anterior surface of the iris (5 *B*). The next rabbits used were killed nineteen days after reinoculation of the eyes. These rabbits already showed clinical evidence of tuberculous inflammation. Histologically the eyes showed diffuse infiltration of the iris and ciliary body, with serous exudates and cells, including lymphocytes, leukocytes, epithelioid cells and large mononuclears (fig. 6 *A*), and beginning invasion of the cornea (fig. 6 *B*). Rabbits killed forty-five days after reinoculation showed more advanced disease, tubercles being present throughout the an-

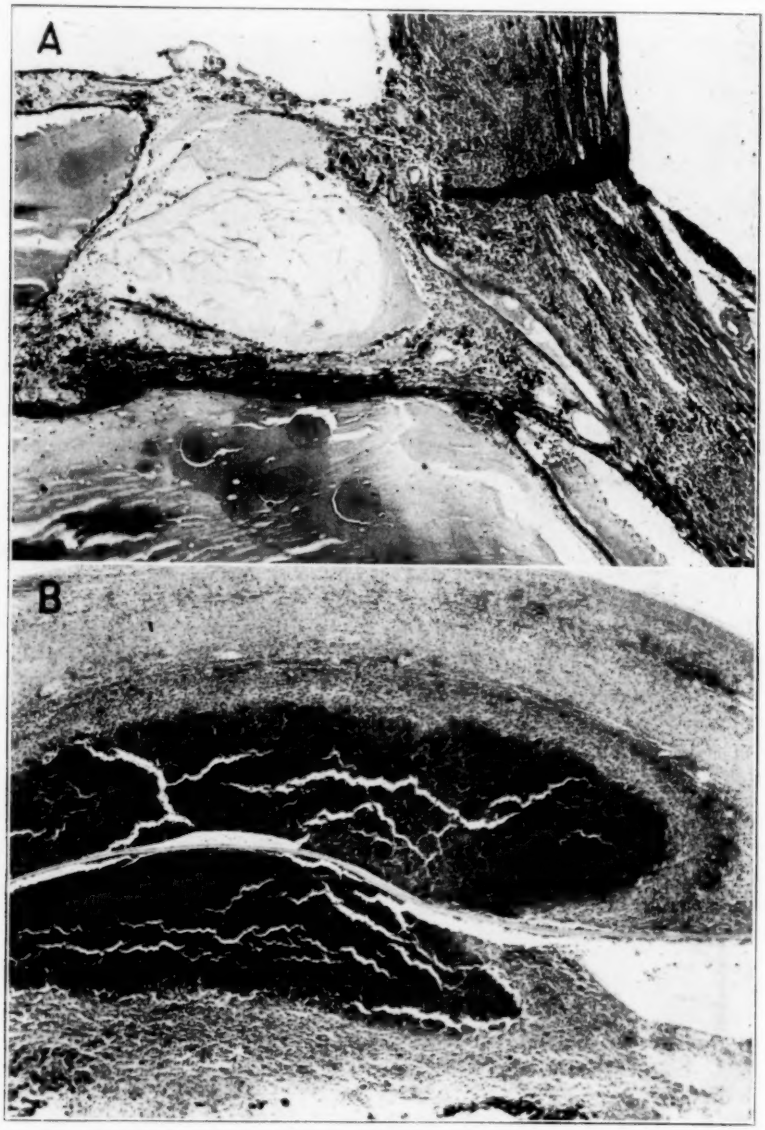

Fig. 7.—(*A*) Well marked tuberculosis of the iris, ciliary region and cornea, with early necrosis, forty-five days after reinoculation, and (*B*) large caseating tuberculoma of the cornea and the root of the iris seventy-seven days after reinoculation, in immune-allergic rabbits with old healed secondary ocular tuberculosis. × 50.

terior uveal tract and cornea, with early necrosis (fig. 7 *A*). Rabbits killed late in the experiment, seventy-seven days after reinoculation, showed advanced disease, with pronounced corneal involvement, caseation and necrosis. Figure 7 *B* shows a large necrotic, but somewhat atypical, tuberculoma, involving both the iris and the cornea at the angle of the anterior chamber.

COMMENT

The one positive result in these experiments is the observation that the resistance to reinoculation manifested by recently recovered eyes is a transitory phenomenon. It appears to be related to the presence of macrophagic cells in the ocular tissues. When the tuberculous foci become inactive, the cellular infiltration becomes less, and the eyes show only what might be called "nonspecific scarring;" then the resistance to reinoculation vanishes. Since one can apparently rule out other obvious factors, it appears logical to conclude that the resistance shown to reinoculation by clinically recovered eyes is related to the persistence of active, but subclinical, tuberculous disease. In other words, the idea formerly entertained that an attack of ocular tuberculosis might endow the eye with a local tissue immunity was a chimera. The immunity which existed was transitory and was a cellular phenomenon, dependent probably on the premobilization of macrophagic cells. It is possbile there may have been the additional factor of help from the circulating antibodies, present in the eye in greater concentration as a result of the increased vascularity, but there is no actual evidence on this point. These experiments, therefore, throw no additional light on the nature of immunity, but do confirm the generally held view that in its essence immunity is due to a cellular and humoral reaction.

Barren as this study is of any substantial advance in knowledge, the experimental data recorded give food for thought on the general question of ocular tuberculosis. Comment has already been made on the similarity of experimental ocular tuberculosis in the rabbit to the tuberculous ocular lesions in man with respect to the clinical picture and course of the disease. The demonstration that in experimental ocular tuberculosis subclinical tuberculous lesions smolder in the eye well after the time that all clinical evidence of activity has disappeared is of considerable interest. Also of significance is the observation that in the desensitized group of rabbits reported on in study VII, when tuberculin therapy was stopped, the sensitivity recurred in 4 of 11 eyes which had clinically inactive disease, and the eyes again became acutely inflamed and ruptured.

In the experimental disease the general picture of recovery, with subsequent healing or relapse, appears to be somewhat as follows: As the local tissue sensitivity subsides, either as a result of tuberculin therapy or incidental to a fortuitous decrease in the severity of the disease, the acute inflammatory phase of the process subsides, and the clinical evidences of active inflammation disappear. A phase in which there is apparent recovery, with low tissue sensitivity, follows, but there is still a smoldering and restrained subclinical tuberculosis, with cellular infiltration of the affected tissues. During this phase any new bacilli arriving in the eye find here a low sensitivity and produce little inflammatory reaction. The bacilli are probably promptly phagocytosed by the premobilized macrophages and epithelioid cells. Thus, the eyes for a time appear relatively immune. Thereafter the ocular disease may follow one of two courses, the direction being dependent on such imponderables as the general resistance of the animal and the individual tendency toward hypersensitivity. On the one hand, the subclinical lesions may gradually become encapsulated, the cellular infiltration diminish and disappear and the eyes actually heal, with variable amounts of scarring. In some eyes viable bacilli may still be present, and the essence of the healing in such eyes is probably bacteriostasis, and not complete destruction of the organisms. If the immunity should fade in such animals, the viable bacilli may multiply, with recurrence of the ocular inflammation. In other animals, in which good immunity does not develop, the bacilli in the subclinical lesions may gradually multiply, the tissue sensitivity recur and, with return of the local sensitivity, a relapse of the disease occurs with acute inflammation, necrosis and caseation. There is apparently no such thing as local tissue immunity.

If this concept of the process is applied to ocular tuberculosis in man, there are obvious lessons to be learned. The apparent healing of a tuberculous lesion, with subsidence of clinical evidences of activity, should not be regarded with too much complacency or undue satisfaction. It must be realized that the eye has passed only into the first phase of the actual healing process, however elated both the patient and the physician may be with the apparent recovery. Efforts should be continued to promote the general health and resistance of the patient and to prevent the recurrence of tissue hypersensitivity. The significant experimental observation on this point is the fact that within one year after cessation of tuberculin therapy, sensitivity recurred, the immunity declined and the bacteria began to grow in 4 of 11 desensitized and apparently

healed rabbit eyes, and that with this return of sensitivity there was renewed ocular inflammation, with caseation and necrosis. It is quite possible that, with further passing of time, the same process might have occurred in other rabbits of this group. Such an experimental result, if applied to clinical ophthalmology, is a definite indication that tuberculin should be continued for a long period in order that relative tissue insensitivity may be maintained. Unfortunately, the phenomenon of immunity is far from being completely understood.

SUMMARY

An experimental study of the increased resistance manifested by the eyes of rabbits which had recently recovered from an attack of ocular tuberculosis revealed that this increased resistance was transitory, gradually diminishing after four months and completely absent after one year. It was not related to enhancement of the general immunity, to a decrease in the reaction capacity of the eyes or to the increase in vascularization resulting from the former infection.

It was found that eyes which had every clinical evidence of subsidence of all active inflammation still showed smoldering tuberculous foci and cellular infiltration when examined microscopically. As these eyes completely recovered and these microscopic evidences of activity faded, the resistance to reinoculation likewise disappeared.

A study of the status of the ocular sensitivity of rabbits which had been almost completely desensitized one year before, and for which tuberculin therapy had been discontinued for one year showed a return of the sensitivity and a recurrence of the ocular tuberculosis in 36 per cent of the animals. On the basis of these experimental results, it is concluded that the resistance to reinoculation in the experimental rabbit with ocular tuberculosis is a transitory and a cellular phenomenon, dependent probably on the premobilization of macrophages.

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LEPTOTRICHOSIS CONJUNCTIVAE

A FURTHER REPORT

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In the discussion on a paper by Hurst, one of us (S. R. G.)[1] summarized the cases of leptotrichosis of the conjunctiva in which a thread mold had been observed in sections in our laboratory, and a case was mentioned in which cultures of the organism were obtained. Other cases have been seen since this time, and it seems worth while to review this material.

REVIEW OF LITERATURE

A brief review of the literature will include only the reports of cases in which the leptothrix, or a thread mold presumed to be the leptothrix, was seen in sections or culture. A discussion of the oculoglandular syndrome of Parinaud has been published elsewhere by Gifford and Dillon,[2] and most American ophthalmologists are familiar with the three diseases which may be grouped under this name: tuberculosis of the conjunctiva, the oculoglandular form of tularemia and leptotrichosis conjunctivae.

The observation of the leptothrix in sections of material from cases of a condition known as Parinaud's conjunctivitis was first made by Verhoeff,[3] in 1913. A special staining technic was necessary to demonstrate the organism, and it was found only when a characteristic area of focal necrosis was excised and the tissue fixed in Zenker's fluid. In his latest report Verhoeff[4] reported having observed the organism in specimens from 54 of 56 cases in which the tissue showed the characteristic histologic picture described by him. He advised the staining of a number of sections with hematoxylin and eosin and selection of one or two sections presenting the characteristic picture of phagocytosis of necrotic material by microphages; these sections are then stained by his modified Gram method without decolorization of the hematoxylin and eosin stain. It is only in this way, he stated, that areas containing the threads may be detected. In material not showing this picture the threads are not seen, and this was true of material from a number of cases submitted to him which were not included in his series. In many instances the material had been submitted to him by other ophthalmologists, and such cases, with Verhoeff's observations, were reported by Keiper,[5] Lemoine[6] and Dunphy.[7]

In 1927, one of us (S. R. G.)[8] reported identification of the organisms in 2 cases, in 1 of which a single large granulation was excised. This was presumed to be the primary lesion, since a foreign body, probably of vegetable origin, was observed embedded in the tissue and surrounded by organisms. Excision was followed by the appearance of other typical areas of focal necrosis, and the condition ran a characteristic course. These 2 cases were the first in which the organism had been seen outside of Verhoeff's laboratory. In 1934 a third case in which the organism was identified was reported by Gifford and Dillon.[2] In 1936 Lamb[9] observed leptothrix filaments in sections from 2 typical cases.

Hurst,[10] in a series of 23 cases of oculoglandular disease, reported the observation of leptotriches in sections from 4 cases. In 2 of these 4 cases, to be referred to later, the identification was made in our laboratory, the observations in the others being made by Dr. Harvey Lamb, of St. Louis, and by Dr. Verhoeff. In this series of cases of oculoglandular disease were 2 instances of oculoglandular tularemia in which agglutination tests gave positive results and 17 cases in which no agent could be seen, although in only 3 of these was tissue removed for study.

† Dr. Gifford died on Feb. 25, 1944.

From the Departments of Ophthalmology and Bacteriology, Northwestern University Medical School.

1. Gifford, S. R., in discussion on Hurst.[10]

2. Gifford, S. R., and Dillon, E. E.: Conjunctivoglandular Syndrome of Parinaud: Report of Case Showing Thread Mold in Sections, Arch. Ophth. **12**: 518 (Oct.) 1934.

3. Verhoeff, F. H.: Arch. Ophth. **42**:345, 1913; **63**:345, 1918; Am. J. Ophth. **1**:702, 1918.

4. Verhoeff, F. H.: Leptotrichosis Conjunctivae (Parinaud's Conjunctivitis) Without Glandular Involvement: Report of Case, Arch. Ophth. **25**:1 (Jan.) 1941.

5. Keiper, G. F.: Ann. Ophth. **22**:780, 1913.

6. Lemoine, A. N.: Parinaud's Conjunctivitis with Demonstration of Leptothrix of Verhoeff, J. A. M. A. **82**:537 (Feb. 16) 1924.

7. Dunphy, E. B.: Am. J. Ophth. **9**:669, 1926.

8. Gifford, S. R.: Am. J. Ophth. **10**:484, 1927.

9. Lamb, H. D.: Am. J. Ophth. **19**:571, 1936.

10. Hurst, V. R.: Am. J. Ophth. **22**:891, 1939.

Early attempts to cultivate the organism were usually unsuccessful. Wherry and Ray [11] cultured material from the preauricular gland of a patient and isolated an unbranched thread mold which, although it was gram-negative, they claimed to be identical with the leptothrix described by Verhoeff. Growth was on Dorset's egg medium under anaerobic conditions. In 1933 Verhoeff and King [12] obtained cultures of the leptothrix in 3 out of 4 cases. They employed excised conjunctival tissue, and growth was positive only on serum agar and dextrose agar under 10 per cent carbon dioxide tension. Sections of tissue in all these cases showed the organism, and subconjunctival injections of organisms grown in culture produced lesions in rabbits. In a later report [4] Verhoeff stated that culture of material from 7 subsequent cases resulted in growth in only 2 cases, though in all but 1 of these cases organisms were present in sections. Verhoeff employed excised tissue for culture and did not aspirate material from the glands. It is noteworthy that in 1 of his cases in which numerous organisms were noted in sections no preauricular adenopathy was present, this being the only case of the kind on record. Culture of material did not yield the organism in this case, and Verhoeff recommended examination of tissue as much more reliable than culture in diagnosis.

In 1937 Wright [13] cultivated leptotriches from fluid aspirated from the preauricular gland in a case. Primary cultures were grown under anaerobic conditions on Soparkar's heated human blood medium at 30 C., hydrocele agar and ordinary agar enriched with a surface smear of human blood. Subcultures were obtained under both aerobic and anaerobic conditions. Wright expressed the belief that culture should be simpler and more reliable for diagnosis than the study of sections. He described the identification of the organisms by Verhoeff's method in sections from typical cases of the disease, but he did not report these cases. The organism isolated by Wright was gram-positive, while that cultured by Wherry and Ray and at least two strains grown by Verhoeff and King were described as gram-negative. In sections the granules in the threads and some of the threads were gram-positive, while parts of the threads are decolorized.

Since the report of Gifford and Dillon, in 1934, material from 14 cases has been examined in our laboratory. Most of the patients were seen personally by one of us (S. R. G.), some having been referred by other ophthalmologists for excision of the material. In all but 2 cases the typical clinical picture described by Verhoeff was noted. Of the exceptions, 1 was a case of oculoglandular tularemia in which positive agglutination reactions were later obtained, and in the other no definite areas of focal necrosis, but only large follicles in the upper fold with adenopathy, were observed. Material alone was examined from 7 cases, submitted by Dr. V. R. Hurst, of Longview, Texas; Dr. W. H. Morrison, of Omaha; Dr. Harold Gifford, of Omaha; Dr. W. M. Scales, of Hutchinson, Kan., and Dr. W. H. Theobald, of Chicago. It is assumed from the histories submitted, and in 1 case from a kodachrome photograph, that all these 7 cases showed the typical clinical picture of Parinaud's oculoglandular syndrome. Hence, except for the 2 cases aforementioned, material was available from 12 cases in which leptotrichosis conjunctivae was, with good reason, suspected.

Without any detailed discussion of the histopathologic changes, it may be said that the specimens in all 12 cases showed the histologic picture described by Verhoeff. In 8 of these cases Verhoeff's modified Gram method revealed granules and threads of a thread mold, presumably leptothrix, in sections, while in 4 cases no such elements could be seen. The 8 cases in which the organism could be identified and the 3 cases already reported make a total of 11 cases in which leptothrix has been identified in sections by one of us (S.R.G.). The organisms were approximately of the same size in all cases, but their distribution in the tissues varied considerably (figure). In several specimens dilated capillaries were filled with granules and threads, an observation not reported by Verhoeff. In other specimens large mononuclear cells contained masses of gram-positive granules, among which short chains of granules could be made out by careful focusing. It requires some familiarity with the appearance of the leptothrix in sections for one to be sure of identification in certain specimens, and it is particularly difficult to photograph the organisms. This, in addition to the necessity of obtaining the essential lesions in the specimen and of a careful staining technic of material fixed in Zenker's fluid, probably accounts for the negative reports in a number of cases.

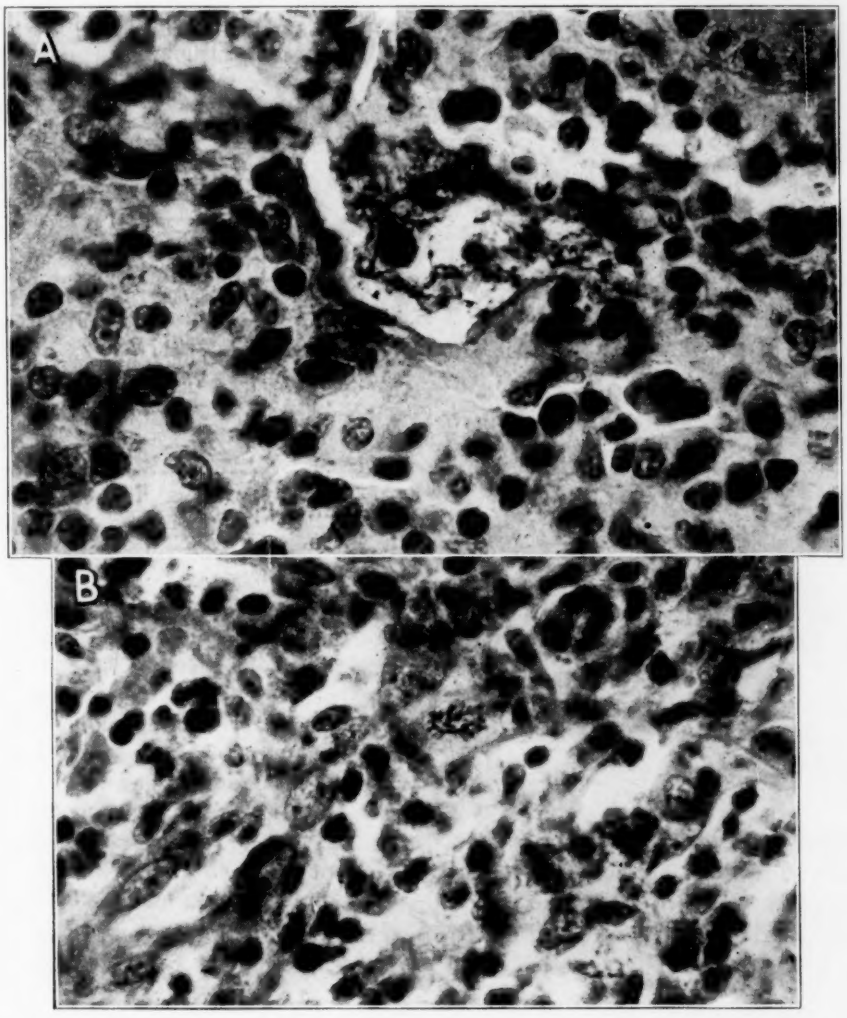
Material was cultured in 3 cases according to the technic described by Verhoeff and King, with the addition of Soparkar's medium, as advised by Wright. In all 3 instances material for culture

11. Wherry, W. B., and Ray, V.: J. Infect. Dis. **22**:554, 1918.

12. Verhoeff, F. H., and King, M. J.: Leptotrichosis Conjunctivae (Parinaud's Conjunctivitis): Artificial Cultivation of Leptotriches in Three or Four Cases, Arch. Ophth. **9**:701 (May) 1933.

13. Wright, R. E.: Isolation of Verhoeff's Leptothrix in Case of Parinaud's Syndrome, Arch. Ophth. **18**:233 (Aug.) 1937.

was obtained by aspiration from a swollen preauricular gland, while in 1 of these cases material excised from the upper fornix was used as well. In only 1 of these cases was the leptothrix grown in culture, the results of culture in 1 of the others being negative and a growth of saprophytes of no significance being obtained in the other. In all these 3 cases leptothrix elements appeared in sections of the conjunctival lesion, and in 1 of the cases in which cultures of material from the gland were negative, so many leptothrix elements were noted in the conjunctival lesions as to make it seem likely that they would have grown in culture if material from such a lesion had been used for this purpose.



Photomicrographs, showing (*A*) leptothrix threads in an enlarged capillary and (*B*) granules and short threads in an epithelioid cell.

Briefly, the characteristics of the leptothrix isolated from a single case were as follows:

The material was a few drops of cloudy fluid aspirated from a swollen preauricular gland. Original inoculation was on human blood agar with the cultures grown under anaerobic conditions, the cultures kept at 10 per cent carbon dioxide tension being negative for the organism. The colonies developed only after seven days' incubation. Subcultures grew aerobically on the usual mediums. Gelatin and blood serum were liquefied, but no fermentation of dextrose, lactose, sucrose or maltose occurred. No hemolysis was produced. Milk cultures became alkaline. The organisms grown in culture were long slender rods and threads, which formed terminal spores after seventy-two hours. They were uniformly gram-negative. This was true of the organisms isolated by Verhoeff and King, although in sections the organisms were gram-positive with Verhoeff's stain, as were ours. It was easy to decolorize them with oil of organum, however, and there seems to be no doubt that the organism obtained in culture was the same as that seen in sections. It may be mentioned

that the strains of leptothrix isolated by one of us (S. R. G.) from a case of a different type of chronic conjunctivitis and from a case of meibomitis were gram-postive in smears and cultures.

Subconjunctival injection of the organism in a sphinx baboon gave no reaction in forty-eight hours. Similar inoculation in a rabbit produced a profuse discharge from and swelling of the conjunctiva. The rabbit died after three days, and the organism was recovered from the conjunctiva in mixed culture. Death was apparently due to an intercurrent infection, as other organisms were grown from the viscera and heart's blood.

naud" and will give an idea of the relative frequency of the diseases in the districts surrounding Omaha and Chicago. Under leptotrichosis conjunctivae are classified only cases from the present and former reports in which positive identification of the threads was made in sections by one of us (S. R. G.), and under the syndrome "of unknown origin," cases in which sections were made but no organisms were seen. A few cases in which no material was removed are not included.

It is evident that, at least in the Middle West, leptotrichosis conjunctivae is much more common

Data on Cases of the Conjunctivoglandular Syndrome of Parinaud

	No. of Cases	Local Signs	Blood Picture	Febrile and Systemic Reactions	Positive Laboratory Findings
Oculoglandular tularemia.....	1	Focal necrosis and ulcers	Leukocytosis	Usually severe	Agglutination of Pasteurella tularensis after 2d week
Tuberculosis of the conjunctiva	1	Usually one ulcer	No change	Usually absent	Acid-fast bacilli in scrapings; positive guinea pig inoculation
Leptotrichosis conjunctivae.....	15	Small areas of focal necrosis; granulation	Eosinophilia, count of 3 to 10% in 50% of cases	Moderate in first week	Elements of thread mold in sections of lesion stained by Verhoeff's method; characteristic histopathologic picture; cultures may be positive for the leptothrix
Conditions of unknown origin..	7	Variable; usually same as in leptotrichosis	Variable	Moderate in first week	None; sections may show histopathologic picture resembling that of leptotrichosis *

* This picture was not noted in Verhoeff's material.

These results make us inclined to agree with Verhoeff that the examination of properly fixed and stained material in sections offers a greater likelihood of obtaining positive identification of the leptothrix than the use of cultures. The value of cultures in addition to sections, however, should not be minimized, as exact identification of the organism in a greater number of cases is certainly desirable.

The accompanying table will perhaps serve to review the salient features of the group of diseases which may be classified under the general name "conjunctivoglandular syndrome of Pari-

than either conjunctival tuberculosis or oculoglandular tularemia. It is probable that with more exact clinical observation and the use of available laboratory methods in every case in which this syndrome is present, the number of cases of the disease classified as "of unknown origin" would be reduced to an even smaller figure than that shown in the table. In every case agglutination tests with Pasteurella tularensis should be employed, and, if the reactions are negative, a piece of tissue containing a characteristic lesion should be fixed in Zenker's fluid and submitted to adequate examination.

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FUNDUS OCULI IN UROLOGIC DISEASES ASSOCIATED WITH SYSTEMIC HYPERTENSION

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NEW YORK

This paper will be limited to the consideration of three urologic diseases associated with hypertension: pyelonephritis, hydronephrosis and polycystic kidney. These diseases may exist independently, or they may be combined. In several patients with one or another of these conditions, who were referred to me during the past year for an ophthalmologic report, examination disclosed various grades of lesions of the fundus.

In reviewing the ophthalmologic literature, I was unable to find any paper on this subject, although Longcope,[1] Weiss and Parker [2] and other internists and urologists in their papers on pyelonephritis and other urologic conditions reported the presence of lesions of the fundus. It is significant to find that in severe urologic diseases with persistent hypertension the changes in the fundus are similar to those observed with essential hypertension, chronic glomerulonephritis, toxemia of pregnancy and, rarely, arteriosclerosis. The question whether the hypertension or the urologic disease or both are responsible for the lesions in the fundus is still an open one. Some urologists and internists have stated that, from their clinical examinations, they believe that the hypertension is secondary to the urologic disease. Accordingly, another question to be considered is whether the high blood pressure existed in these patients as an independent condition (essential hypertension) or whether it was the result of the urologic disease (secondary hypertension). I do not consider urologic disease associated with persistent high blood pressure and lesions in the fundus a clinical entity, but still it is a frequent combination. Any pathologic condition of the kidney, affecting to any extent its blood supply or its urinary drainage, may, if not relieved, cause vascular structural changes, with such a resulting disturbance as renal ischemia. Some authorities consider the renal condition to be the basic cause of hypertension. The hypertension results in arteriolar spasm, sclerosis and other lesions affecting the vital organs, including the fundus oculi. The lesions in the fundus may be progressive or retrogressive. The prognosis of the urologic disease with hypertension rests chiefly on the condition of the vital organs. The signs in the fundus are often the visible guide to the condition of the cardiovascular-renal system.

Read before the New York Academy of Medicine, Section of Ophthalmology, Nov. 15, 1943.

From the Department of Ophthalmology, in cooperation with the Departments of Medicine and Urology, of the New York Post-Graduate School and Hospital.

1. Longcope, W. T.: Chronic Bilateral Pyelonephritis: Its Origin and Association with Hypertension, Ann. Int. Med. **11**:149-163 (July) 1937.

2. Weiss, S., and Parker, F., Jr.: Pyelonephritis: Its Relation to Vascular Lesions and to Arterial Hypertension, Medicine **18**:221-315 (Sept.) 1939.

CLINICAL CONSIDERATIONS

I shall consider briefly some clinical facts pertaining to the urologic diseases mentioned. These diseases are due either to an ascending or descending acute or chronic infection of the urinary passages or to a urinary obstruction, caused by such agents as calculus, stricture, an enlarged prostate or congenital anomalies. A physical examination is obviously required, as well as a report on both kidneys. Examination should include roentgenographic, pyelographic and cystoscopic studies, as well as tests for renal function, examination of urinary smears, determination of the blood pressure and examination of the fundi.

Pyelonephritis.[3]—This disease is an infection of the pelvis and parenchyma of the kidney, which is frequent, especially in children, and is often due to the colon bacillus. It may progress from an acute to a chronic stage and may result in a pyelonephritic, atrophic kidney with extreme hypertension.

CASE 1.—R. S., a man aged 43, a truckman, was admitted to the clinic on March 5, 1943. His physician reported that he had had persistent high blood pressure for the last fourteen months. He was married and had 2 healthy children. He had never suffered previously from any serious disease, but he gave a history of nocturia and transient amblyopia. He complained chiefly of attacks of severe occipital headache, lasting two hours. He had had an attack of Bell's palsy two weeks before admission to the clinic. Medical treatment was of no avail. He was referred to me for an examination of

3. Barker, N. W., and Walters, W.: Hypertension Associated with Unilateral Chronic Atrophic Pyelonephritis: Treatment by Nephrectomy, Proc. Staff Meet., Mayo Clin. **13**:118-121 (Feb. 23) 1938.

the fundus, which resulted in a diagnosis of bilateral neuroretinopathy associated with pyelonephritis.

On April 1 he was transferred to the medical ward of the hospital. An abstract of the hospital record shows that the blood pressure ranged from 200 systolic and 140 diastolic to 180 systolic and 110 diastolic. The renal function was normal. The urine showed mild proteinuria but was otherwise normal, with no colon bacilli or pus cells. Intravenous urographic and retrograde pyelographic examinations revealed a normal condition of the left kidney and lobulation of the right kidney, with uncertain filling of the renal pelvis. These findings suggested the presence of a neoplasm; therefore it was decided, after consultation, to remove the right kidney. The patient's blood pressure was not lowered after the operation, but the headaches were relieved. On May 5 he was discharged from the hospital and was advised to return to the clinic. Microscopic examination of the removed kidney (fig. 2) revealed a wedge-shaped area of scarred tissue, extending to the pelvis of the kidney, as well as sclerosed and narrowed blood vessels. Large foci of mononuclear cells surrounded the vessels. Many glomeruli were hemorrhagic, and others were partly sclerosed. The diagnosis was pyelonephritis of the right kidney and anterior malposition of its pelvis.

Examination of the Fundus: The results of examination a week after nephrectomy were as follows (fig. 1): The lesions were similar to those seen before the operation; they were practically identical in the two eyes. The optic disk and the surrounding area were edematous; the macular area was normal. The retinal veins were uniformly congested; they were also compressed and deflected where they were crossed by hyalinized arterioles. The arterioles were narrowed; some were of irregular caliber; others showed a prominent central light reflex. Located near the macular area were numerous glistening, sharply defined, whitish foci, the result of lipid degeneration. Similar foci of lipid material were also present above and nasal to the disk. A large whitish retinal plaque was located in the vertical meridian, at some distance below the disk. This was caused by a lymphocytic exudate and was surrounded by hemorrhages. Flame-shaped hemorrhages were visible above and below the disk. The diagnosis based on the appearance of the fundus was bilateral neuroretinopathy accompanying pyelonephritis, with hypertension.

Subsequent Course: A recent ocular examination at the clinic, on September 23, revealed the following status: Vision remained 20/30 in each eye, as noted prior to the operation. Neuroretinal edema was now increased. The blood pressure was 230 systolic and 130 diastolic; the excruciating headaches had returned; renal function was normal, and proteinuria was present.

The case came up for discussion at a medical conference at the hospital on September 23. The general impression was that the pyelonephritis preceded the hypertension and the lesion in the fundus. The patient was readmitted to the hospital on October 10 because of continuous severe headaches and persistent high blood pressure. On October 23 the blood pressure was 216 systolic and 102 diastolic; the urea nitrogen was 46 mg. and the creatinine 4 mg. per hundred cubic centimeters, values indicative of renal involvement. Vision was the same as that previously noted. Additional changes had developed in the fundus: Papilledema of 3 D., as well as profuse fresh retinal hemorrhages with exudates, was present in the right eye; changes in the left eye were similar except that the elevation of the disk measured 2 D.

On October 30, because of the persistent excruciating headaches, a bilateral splanchnic sympathectomy (Smithwick[4]) was performed. A week later the elevation of the disks had subsided, while the retinal changes remained the same. The blood pressure was 172 systolic and 108 diastolic; the urea nitrogen measured 33 mg. and the creatinine 3.2 mg. per hundred cubic centimeters, a decrease indicating reduction in the hypertension and improvement in renal function.

In a review of this case, it is evident that the nephrectomy and the absolute rest of seven months had no beneficial effect on the secondary hypertension. The increased lesions in the fundus and the impairment of renal function indicated progression of the underlying disease. The sympathectomy improved the renal function and reduced the hypertension, as well as the edema of the disk. It is obviously too soon after the sympathectomy for any prognosis with regard to the outcome in the case.

I noted a similar case of unilateral pyelonephritis with nephrectomy in a paper published earlier this year.[5]

Hydronephrosis.[6]—CASE 2.—M. R., a man aged 43, a merchant, was married and had 2 healthy children. Physical examination showed a normal condition except for pain over the lower part of the spine and foul, bloody urine. The patient first consulted a physician in 1931 and had been examined at intervals since. In 1935 an excretory urogram showed nothing abnormal. Cystoscopic examination showed a tumor at the neck of the bladder, and a suprapubic excision was performed. The microscopic diagnosis of the growth was carcinoma, and radium seeds were planted in the bladder. After a few weeks pyelonephritis developed on the right side, as a result of infection of the bladder, and nephrectomy was required. In February 1937 the patient reentered the hospital for a check-up. Pyelograms taken at this time revealed bilateral hydronephrosis. A cystoscopic examination disclosed no recurrence of the carcinoma. He was discharged and advised to report to his physician at regular intervals.

On Jan. 14, 1943 I examined the patient for the first time, because of sudden blurring of vision. Vision was 20/30 in the right eye and 3/200 in the left eye. Functional tests, including measurement of intraocular tension, gave normal results. His blood pressure was 260 systolic and 140 diastolic, and there were pronounced lesions of the fundus. He then consulted his physician, who referred him to the hospital, on Jan. 18, 1943, for reexamination and treatment. Studies then showed poor excretory function in both kidneys and moderate increase in the urea content of the blood (25.3 mg. per hundred cubic centimeters), associated with diminution of vision and pronounced hypertension. The patient was discharged four days later. The urologic diagnosis was bilateral hydronephrosis with hypertension.

4. Smithwick, R. H.: A Technique for Splanchnic Resection for Hypertension, Surgery **1**:1-8 (Jan.) 1940.

5. Cohen, M.: Fundus Oculi in Hypertensive Vascular Diseases, Arch. Ophth. **29**:85-91 (Jan.) 1943.

6. Keith, N. M., and Pulford, D. S., Jr.: Experimental Hydronephrosis: Functional Anatomic Changes in the Kidney Following Partial Ureteral Obstruction, Arch. Int. Med. **20**:853-878 (Dec.) 1917.

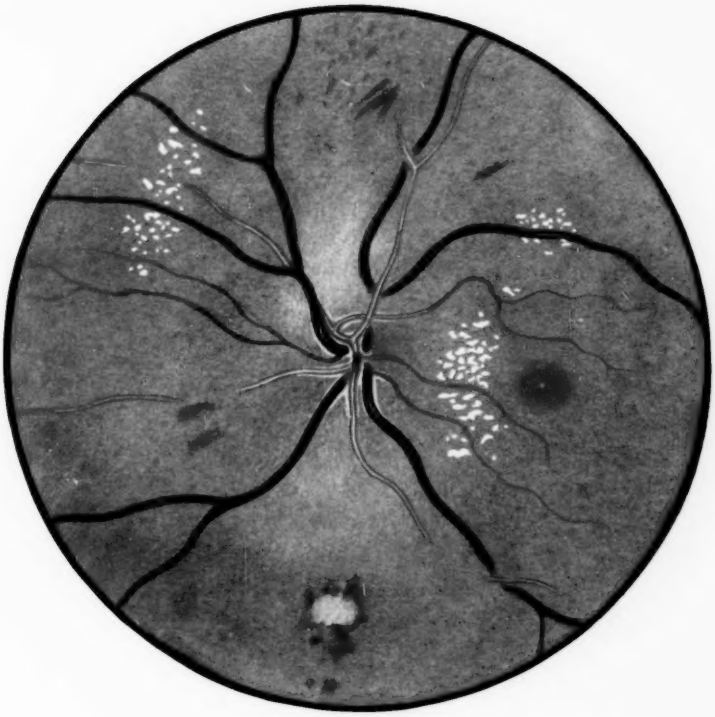

Fig. 1.

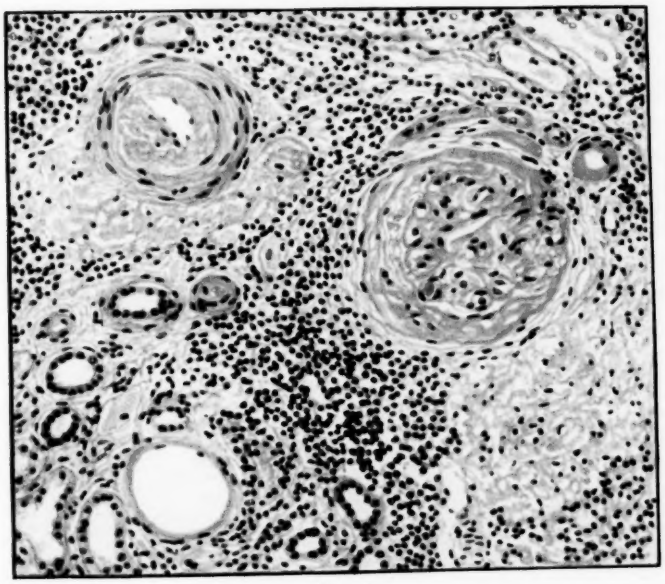

Fig. 2.

Figs. 1 and 2 (case 1).—*1*, appearance of the fundus, and, *2*, microscopic appearance of the diseased kidney, in a case of pyelonephritis.

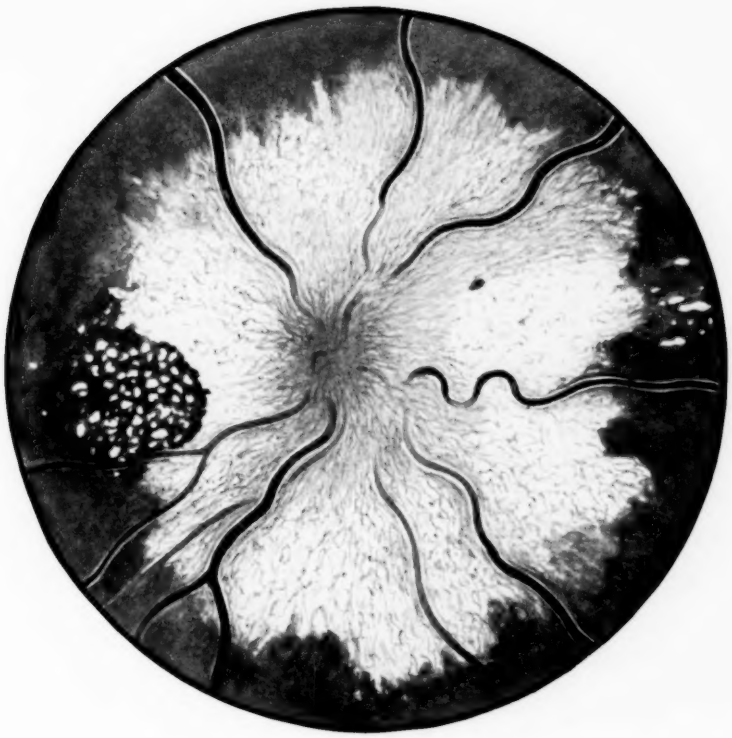

Fig. 3.

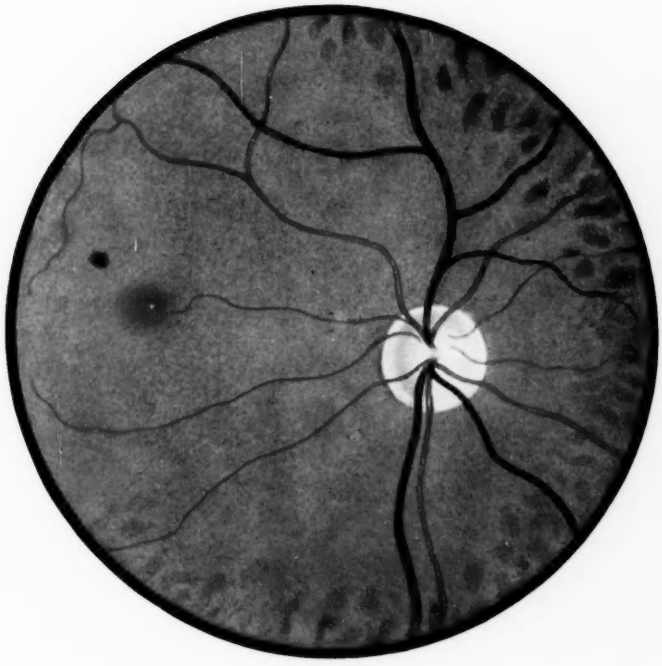

Fig. 4.

Figs 3 and 4.—*3*, fundus of the right eye in a case of hydronephrosis, and, *4*, fundus of the eye in a case of polycystic kidney.

Examination of the Fundus: The changes in the fundus were as follows (fig. 3): In the right eye, the optic disk was hyperemic and its margin blurred. The disk was completely surrounded by a large whitish patch, which was mottled, with threadlike, brownish markings, and had a sharply indented margin. Retinal vessels crossed the patch. These changes may indicate a preexisting extensive exudate, which, on being resorbed, left the diffuse whitish scar. The macular area was made up of glistening lipid dots surrounded by pigment. Lipid foci were also seen in the periphery of the fundus. The retinal veins were tortuous and bordered by white lines, a condition indicating periphlebitis. The arterioles were mostly obscured; a single arteriole was visible below the disk. There was a small circular hemorrhage in the whitish patch. The diagnosis based on the appearance of the fundus was neuroretinopathy, with a large peripapillar exudate associated with hydronephrosis. In the left eye, the disk was edematous, and the macular area showed chorioretinal foci of degeneration. The retinal veins were moderately engorged; they were tortuous, and some were compressed by sclerosed arterioles. Many arterioles were obscured, and those which were evident were narrowed. The central light reflex in some vessels was prominent. An isolated retinal hemorrhage was located above the disk. The diagnosis based on the appearance of the fundus was neuroretinopathy associated with hydronephrosis, with hypertension.

Subsequent Course: On October 11 I reexamined the patient. He now complained of deterioration of his general health. Inspection of the fundi showed an increase in the retinal lesions, and the blood pressure was also elevated.

Since the patient had been free from hypertension before the onset of most of the urologic symptoms, it may be assumed that the hypertension followed the renal involvement and that the urologic treatment produced no beneficial results. This was evident from the sustained high blood pressure and the increase in the lesions of the fundus, which suggested a grave prognosis.

Polycystic Kidney.[7]—CASE 3.—N. L., a man aged 34, a salesman, was married and had 1 healthy child. He appeared well nourished and had never suffered from any serious disease before the present hematuria. He stated that his father and a brother died of polycystic kidney. In 1928, in the course of his being examined for insurance, proteinuria and hypertension were discovered. Roentgenographic and cystoscopic examinations at that time revealed nothing significant. He had been admitted to the hospital on four occasions because of gross hematuria, the first visit being in November 1932. At that time his blood pressure was 176 systolic and 130 diastolic, and study of the eyegrounds showed chorioretinal arteriosclerosis. Urinalysis revealed pronounced proteinuria, but the urea nitrogen content was normal. The second admission was in December 1934, for another attack of hematuria. The blood pressure was then 180 systolic and 130 diastolic; urea nitrogen was 43 mg. and creatinine 3.2 mg. per hundred cubic centimeters. He had normal vision.

Examination of the Fundi (fig. 4): The disk was pale, due to sclerosis of the capillaries on the disk. The margin was sharply outlined. The macular area was normal, as were the retinal veins. The arterioles were narrowed. There was a small circular retinal hemorrhage in the periphery of the right fundus. In the outer zone there was an area of retinal depigmentation, which allowed visualization of the choroidal stroma. This area was possibly the result of localized sclerosis of the choriocapillaris. The appearance of the fundus was practically the same in the two eyes. The diagnosis based on the condition of the fundus was bilateral chorioretinal arteriosclerosis, with hypertension.

The third admission occurred in January 1936, after an attack of gross hematuria, with a blood pressure of 184 systolic and 128 diastolic. In June 1936, after another attack of hematuria, preceded by a chill and abdominal pain, the patient was admitted to the hospital for the fourth time. The blood pressure was 172 systolic and 110 diastolic. An intravenous urogram revealed notable enlargement of both kidneys. A retrograde pyelogram showed the typical bilateral renal changes of polycystic disease, with marked dilatation of both the pelvis and the calices. There were profound anemia and definite proteinuria, with innumerable red blood cells. Urea nitrogen was 76.1 mg. per hundred cubic centimeters. An abdominal examination disclosed a palpable mass in the left costal area, and resistance, suggestive of a mass, was also felt on the right side. The diagnosis was polycystic renal disease and azotemia. In 1937, after another attack of hematuria, the patient was admitted to another hospital. According to the records there, his blood pressure at that time was 172 systolic and 128 diastolic. The urea of the blood was 197 mg. per hundred cubic centimeters. Examination of the fundus showed only a small circular retinal hemorrhage in the right fundus. The patient died of retention uremia, five days after admission.

In this case it is significant that the continuous high blood pressure and the disturbance of renal function for at least four years caused no neuroretinopathy in either fundus but simply bilateral chorioretinal arteriolosclerosis. The diagnosis of chronic glomerulonephritis was considered in this case, but, because of the absence of neuroretinopathy for so long a period, with hypertension and azotemia, I believe that this diagnosis was untenable, except in its terminal stage.

SUMMARY

The purpose of this paper is to call to the attention of ophthalmologists the lesions in the fundus associated with urologic diseases. Some internists and urologists have reported the presence of such lesions in connection with these conditions.

Bilateral neuroretinopathy, possibly of inflammatory origin, was the condition in the case of pyelonephritis and that of hydronephrosis reported here, while in the case of polycystic kidney the diagnosis was bilateral chorioretinal arteriolosclerosis of noninflammatory origin.

Further investigation is necessary to ascertain whether inflammatory or noninflammatory lesions

7. Schacht, F. W.: Hypertension in Cases of Congenital Polycystic Kidney, Arch. Int. Med. **47**:500-509 (March) 1931.

occurring with urologic disease produce corresponding lesions of the fundus.

It can be stated that urologic diseases, accompanied by persistent high blood pressure, usually lead to lesions of the fundus.

The changes in the fundus, as revealed by the detailed study of these cases, are indicative of the severity of the underlying hypertensive vascular disease, regardless of the factor or factors responsible for the elevation of the arterial tension.

A report on the examination of the fundus should accompany the records of cases of urologic diseases with persistent hypertension, as it is an additional aid to the diagnosis and prognosis of the disease.

29 East Sixty-Fourth Street.

DISCUSSION

DR. ARTHUR M. FISHBERG, New York: The presence of hypertensive neuroretinopathy in a case of undoubted primary renal disease proves beyond cavil that renal disease itself can cause lesions of the fundus. However, all the evidence indicates that the only way in which renal disease can cause these lesions is through the mediation of high blood pressure; there are no changes in the fundus. The incidence of retinal lesions in any renal disease strictly parallels the elevation of the blood pressure; moreover, it parallels the elevation of the diastolic, and not the systolic, pressure. Even with the most pronounced elevation of systolic pressure there will be no retinal lesions as long as the diastolic pressure is not elevated. The best evidence of this is derived not from cases of renal disease but from those of aortic regurgitation in young people who run high systolic pressures, even close to 300 mm. of mercury, for years without a rise in diastolic pressure, and never have lesions of the fundus. The evidence is clear; the parallelism is with the diastolic pressure. Any measure that reduces the diastolic pressure is likely to result in clearing up of the retinal lesions. Good examples are seen in cases of toxemia of pregnancy and in those of successful sympathectomy; when the blood pressure is reduced, the retinal lesions improve or clear up altogether. It may thus be said to be definitely established that the elevation of diastolic pressure in some way produces the retinal lesions, but I cannot state how. Since the days of Volhard it has been conventional to say that it is due to angiospasm in the retina.

For a time it seemed probable that the elevation of intracranial pressure might be connected with lesions of the fundus. Pickering showed that of 23 cases of malignant hypertension, the cerebrospinal fluid pressure was definitely elevated in 22, but I doubt whether this in itself could be the cause of the papilledema and the retinal lesions. The evidence comes from another branch of pathology. Whenever there is elevation of venous pressure, due either to heart failure or to mediastinal compression, there is always a corresponding elevation of cerebrospinal fluid pressure. No matter how high the venous pressure rises, it is always exceeded by the cerebrospinal fluid pressure. Whenever there is such a pure elevation of cerebrospinal fluid pressure, there is never papilledema or other retinal lesion. Friedfeld and I reported on 70 patients with heart disease, none of whom had retinal lesions or papilledema, and in patients with mediastinal tumors we found corresponding elevations of the cerebrospinal fluid pressure, without any changes in the fundus. Internists who attribute the papilledema in cases of malignant hypertension solely to an increase in the cerebrospinal fluid pressure do not have the entire explanation.

Another point that I wish to stress is the importance to the ophthalmologist of the concept of malignant hypertension. Malignant hypertension is not a disease, but a clinical picture that can result in any form of high blood pressure, providing the blood pressure rises high enough for a sufficiently long time. It occurs with glomerulonephritis, with the Cushing syndrome, with pyelonephritis and with other urologic conditions described by Dr. Cohen. In each of these diseases one can differentiate a malignant phase of the hypertension, that is, a malignant phase of essential hypertension, of glomerulonephritis or of pyelonephritis. The ophthalmologist makes his diagnosis on the basis of the clinical picture produced by the increased diastolic pressure. Papilledema and exudates mean that this particular form of hypertension has entered the malignant phase. They indicate that at autopsy rapidly progressive changes in the arterioles—arteriolar necrosis and so-called endarteritis—will be encountered. There is a tendency to the rapid deterioration of renal function, so that a large percentage of patients with this condition die in uremia. The presence of cotton wool exudates and papilledema demonstrates that the disease has entered a phase in which the elevated diastolic pressure is acutely affecting the blood pressure in various organs, including the kidney, where it does its greatest damage.

DR. HERMAN ELWYN, New York: I enjoyed the discussion by Dr. Fishberg. In speaking of hypertension, one should always signify the kind meant, whether essential or of renal origin.

The benign phase of essential hypertension has no changes in the fundus. There is no arteriospastic contraction anywhere in the body. The Goldblatt experiment is not represented here. There is nothing but high blood pressure, which may bring on later complications.

Something has been added when essential benign hypertension, which has existed for ten or twenty years, suddenly becomes malignant.

This something is the general arterial contraction in many organs, including the kidneys, the brain and the eyes. This contraction is responsible for the high diastolic pressure and the change from benign hypertension to malignant disease.

Hypertension of renal origin is always secondary to an endangered filtration pressure. The Goldblatt experiment is just that; here a clamp on the renal artery endangers the normal intraglomerular filtration pressure. In consequence, there is a general arterial contraction, and renal hypertension is always the result. Arteriospastic contractions cause changes in the terminal vessel units, with the resulting peristatic and prestatic conditions, followed by the manifestations of retinal changes. It is important to differentiate between essential hypertension in the benign stage and the hypertension which is caused by arteriospastic contraction. It is the latter which produces the retinal changes.

Dr. Arthur M. Fishberg, New York: If the renal arteries are only slightly constricted in the Goldblatt experiment, there result a certain elevation of blood pressure and a perfectly comfortable dog. The animal does not suffer subjectively from a blood pressure of 200 systolic and 120 diastolic, but if the clamp is tightened so that the pressure is sent to very high levels, the dog becomes very uncomfortable, and everything about him reminds one of what is called malignant hypertension in man. The same mechanism which first produces benign hypertension later causes malignant hypertension, and if the investigator releases the clamp, the hypertension returns to the benign stage. There are cases in which the disease in man acts just like that, with the malignant hypertension dependent on the development of a high diastolic pressure.

In a man of 70 the typical picture of malignant hypertension practically never develops because his aorta is sclerotic; the maintenance of a high diastolic pressure requires elasticity of the aorta, which is absent in a person of that age.

In a large number of cases sympathectomy changes malignant hypertension to what one must call benign hypertension for a considerable period, until the effects of the operation wear off.

I can see no reason for saying that a man has acquired a new disease when malignant hypertension develops after five or eight years of high blood pressure; everything indicates that the "malignant hypertension" is merely an aggravation of the disease that has been present for many years.

Clinical Notes

RHINOCANALICULAR ANASTOMOSIS

RICHARD WALDAPFEL, M.D., GRAND JUNCTION, COLO.

The debates on operations on the tear passages appear, for the most part, to be concluded. Each operator has settled down with the method which he likes best and apparently does not find it necessary to add anything new. Yet the procedure which was recently reported by Blumenfeld [1] is so unique and original that it necessitates a brief discussion.

Blumenfeld reported a case in which, after four previous operations on the tear sac, two fistulas formed in the skin, 0.5 cm. medial to the inner canthus. These fistulas represented the distal openings of the upper and lower canaliculi. He excised an oval piece of skin containing the two fistulas. Then, through a window in the bony lateral nasal wall, he exposed the nasal mucous membrane, incised it longitudinally and inserted the oval flap of skin, with the canaliculi attached,

Fig. 1.—Sketch of the tear sac, with both the canaliculi and the first part of the nasolacrimal duct. The black bands represent the different sites of obstruction of the tear passages: (*a*) in the canaliculi; (*b*) in the upper part of the tear sac, near the openings of the canaliculi, and (*c*) in the lower part of the tear sac and the nasolacrimal duct.

into this opening in the nasal mucous membrane. He then joined the edges of the cutaneous flap to the edges of the nasal mucous membrane by stitches, so that a communication of the fistulas with the nasal cavity was established. The primary incision in the skin was then completely closed.

It seems to me that this method, if it proves satisfactory in other cases, should have a place in the surgery of the tear passages. It is not suitable, however, in all cases of chronic suppurative dacryocystitis, as Blumenfeld anticipated, but only in certain cases, which can be selected rather simply.

Obstruction in the tear passages may be situated in the following places: in the canaliculi; in the upper part of the lacrimal sac, adjacent to the canaliculi, or in the lower part of the sac and the nasolacrimal duct. These sites are designated as *a*, *b* and *c* in figure 1. The most frequent occurrence of obstruction in 85 per cent of cases is at *c*. In order to determine the site of obstruction, the canaliculus test is used. When the

Fig. 2.—L. N., aged 61, with chronic dacyrocystitis, epiphora of the right eye and a fistula, 0.5 cm. below the inner canthus, of several years' duration. *A*, appearance before the operation. Fluid injected into the lower canaliculus passed through the fistula and the upper canaliculus (positive canaliculus test). *B*, appearance three days after intranasal dacryocystorhinostomy. The epiphora was completely gone, and the fistula was closed, without any external operation. The result is permanent, after two years' observation.

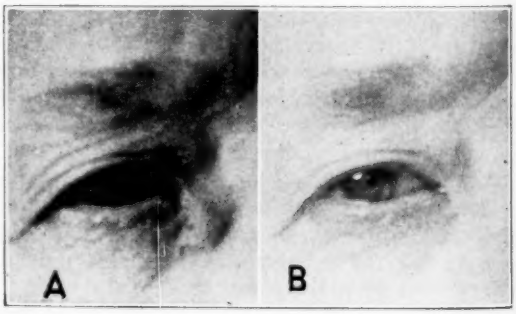

Fig. 3.—C. H. T., aged 70, with chronic dacryocystitis and swelling of the region of the tear sac which frequently was much larger than the picture shows. Epiphora and secretion of pus were present. *A*, before operation, with a positive canaliculus test, and *B*, one day after intranasal dacryocystorhinostomy. The epiphora and swelling were completely gone, without any external operation. The result is permanent, after three years' observation.

1. Blumenfeld, L.: Rhinocanalicular Anastomosis with Reconstruction of the Lacrimal Sac, Arch. Ophth. **31**:248 (March) 1944.

obstruction is at *c*, irrigation of the lower canaliculus will cause the fluid to pass through the upper canaliculus—a positive canaliculus test. When the obstruction is at *a* or *b*, no fluid will pass through the upper canaliculus—a negative canaliculus test. When the canaliculus test is positive, dacryocystorhinostomy is indicated, no matter whether a fistula exists or not. This operation reestablishes normal physiologic conditions by providing for conduction of the tears from the tear sac into the nose, above the stenosis. The fistula closes automatically as soon as the drainage into the nose is instituted without any external operation. Figure 2 shows the appearance of a patient with a fistula before and after the dacryocystorhinostomy. The fistula, which had existed for years, was completetly closed three days after the operation.

The same results are obtained with all swellings in the region of the tear sac in cases of chronic dacryocystitis in which the canaliculus test is positive. The swelling disappears automatically as soon as the drainage in the nose is established, without any external operation. Figure 3 shows such a swelling below the right internal canthus, which had existed for several years and which disappeared immediately and permanently after the dacryocystorhinostomy. In all cases represented by figures 2 and 3, excision of the fistula or the sac is unnecessary. In such cases the dacryocystorhinostomy is, and remains, the method of choice.

Blumenfeld's objections to this operation (West; Toti; Mosher; Halle) are not justified. The statistics for this operation are based on thousands of cases, and the results are analogous to those in the 2 cases illustrated here, successful and satisfactory, with no postoperative manipulations required. The operation offers a cure in almost 100 per cent of cases—if it is properly performed and the cases are carefully chosen, i. e., only those in which the obstruction is at *c*.

The conditions in cases with obstructions at *a* and *b* are different, however. There the dacryocystorhinostomy is not indicated, and other procedures, including extirpation of the tear sac, are often unsatisfactory. It is in such cases, with a negative canaliculus test, in which I see the important field for the new method, a procedure which may fill a gap in the surgical treatment of the lacrimal system.

I think that this clarification is necessary in the interest of the existing valuable methods of operation, as well as in that of the cleverly designed new procedure, in order that it may be accorded the place it deserves.

De Merschman Gardens.

ABSTRACTS OF ARTICLES PUBLISHED IN THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION UNDER THE AUSPICES OF THE SECTION ON OPHTHALMOLOGY, 1943

W. ZENTMAYER, M.D.
PHILADELPHIA

Eye Manifestations of Head Injuries. D. J. Lyle, M.D., Cincinnati, J. A. M. A. **123:** 873 (Dec. 4) 1943.

The subject of ocular manifestations of head injuries is discussed under the headings: concussion, contusion of the brain, laceration, compression and hemorrhage.

The text is illustrated by several case histories.

Most of these injuries fall into three classes: (1) automobile and other travel accidents, which are increasing; (2) industrial accidents, which are multiplied by the acceleration of production to meet the war demands, and (3) head injuries of the war itself.

DISCUSSION

Dr. A. D. Ruedemann, Cleveland: There is a large variety of head injuries. The earliest is that of compression occurring at birth. With the use of forceps, pressure is a factor in the production of hemorrhages at the base of the skull and accounts for a number of cases of squint. Industrial injuries and accidents often involve the head. Severe intermittent headache subsequent to head injury is an excellent diagnostic symptom when most ocular signs disappear. The force of the blow on the orbit may produce a compression fracture in the canal, which can be revealed by the planograph method of roentgenography. Pulsating exophthalmos results from fracture of the base which produces a tear of the internal carotid artery and the cavernous sinus.

Gunshot wounds in the occipital region may give bizarre changes in the visual fields without alterations in the fundus.

Dr. C. W. Rutherford, Indianapolis: War wounds are of greater value to research than those encountered in civilian experience because many more of them are available at one time and they can be studied in groups of cases by specially trained investigators. The studies of Holmes and Lister may be mentioned in this connection (*Brain* **39:** 34, 1918).

Dr. W. I. Lillie, Philadelphia: The importance of pupillary changes should be emphasized, as Dr. Lyle did. Patients with fracture of the skull usually have normal ocular signs during their stay in the hospital but may show ocular damage later. The syndrome of traumatic intracranial changes is not unlike that produced by vascular, inflammatory and neoplastic lesions, although the localizing signs may be masked in the earlier stages of convalescence.

Intraocular Foreign Bodies. E. Stieren, M.D., Pittsburgh, J. A. M. A. **123:** 880 (Dec. 4) 1943.

Every patient with an ocular injury of the globe or the soft parts of the orbit should be given an immunizing dose of 1,500 units of tetanus antitoxin, both for its specific effect and for its action as a foreign protein.

When the foreign body lies in the lens, the latter should be removed at the same time by thorough washing of the anterior chamber. If the wound of entrance involves the ciliary body, the eye is to be enucleated immediately. A metallic foreign body is removed through the cornea when it is anterior to the posterior capsule of the lens, and through a scleral incision when it is in the vitreous, in the choroid or on the optic disk. A hand magnet is always used, with only the cone-shaped or the olive-shaped tip.

The magnet should never be used as a diagnostic instrument. A live magnet should never be brought to the eye. Before the conjunctival flap is sutured in place a cotton-tipped applicator dipped in pure phenol is touched to the scleral wound to prevent postoperative detachment of the retina.

In case of a fairly large piece of copper, brass, coal, stone, wood or lead shot, with the aid of a localization chart and an adequate scleral opening, the forceps (properly designed) are opened and the foreign body is removed. This may require several attempts and may damage the integrity of the eye. Small shot are now made of chilled steel and are therefore magnetic.

DISCUSSION

DR. E. S. SHERMAN, Newark, N. J.: Dr. Stieren's practice of enucleating immediately every eye in which the wound of entrance involves the ciliary body is unnecessarily radical. If the eye is not blind, one should wait a week before enucleating it. In the meantime active foreign protein therapy will often give gratifying results. The fear of retinal detachment following transscleral extraction is exaggerated.

DR. C. A. VEASEY SR., Spokane, Wash.: In cases in which the action of a foreign protein alone is desirable, typhoid vaccine is usually used. If the wound of entrance is through the ciliary body, enucleation is recommended. A few patients have refused to undergo operation and have escaped trouble, but delay is dangerous.

DR. G. H. CROSS, Chester, Pa.: Steel is now combined with many substances which render it less magnetic, so that there are more cases in which nonmagnetic foreign bodies are to be removed. There need be no groping in removal of such foreign bodies. With the assistance of a good roentgenologist and the use of the method which I devised in 1926, it is possible to apply scleral forceps and remove nonmagnetic bodies from the eye with a minimum of trauma even when no view of the interior of the eye is obtainable. When the foreign body is in the lens, sufficient time should be allowed for the lens to become thoroughly opaque, and then an intracapsular operation should be done by the Knapp method. Glass in the anterior chamber sometimes can be removed under high magnification and sharp illumination by grasping the glass fragment with a pair of fine needle point forceps.

DR. E. STIEREN, Pittsburgh: As there is no way of determining in which of the cases with injury of the ciliary body sympathetic ophthalmia may develop, one assumes a tremendous responsibility in retaining the eyeball. Even with use of the fluoroscope there must be more or less disturbance of the vitreous as the forceps are directed to move up or down, to the right or to the left.

Significance of Visual Defects in War Production Effort. H. S. KUHN, M.D., Hammond, Ind., J. A. M. A. **123:** 1085 (Dec. 25) 1943.

A direct correlation was shown by means of graphs between accuracy and visual perfection and between accidents involving loss of time and defects in visual performance.

The minimal visual standards adopted were simple groupings of the basic visual findings according to the visual demands of job groups; they included (1) uncorrected acuity for distant and for near vision; (2) acuity with the glasses habitually worn, i. e., work acuity; (3) muscle balance for distant and for near vision; (4) stereopsis, and (5) color appreciation. To this basic, minimal information were added such special tests of near vision (e. g., determination of the near point of accommodation and of convergence) as might be needed in selecting eyes for exceedingly intricate work done within 12 inches (30 cm.) of the eye. Physicians in general have an exceedingly important and a direct responsibility in the war production effort.

DISCUSSION

DR. H. GLENN GARDINER, Chicago: This is a graphic representation of what is probably one of the greatest rehabilitation programs brought forward during the war.

DR. T. L. TERRY, Boston: "Determination of minimal visual standards for a given occupation" is neither easy nor exact, as superior mental ability may make up for lower visual standards. Education in all mechanical means of preventing blindness is the answer to one phase of the problem.

DR. M. DAVIDSON, New York: The problem is the organization of effective care of the eyes for the industrial population. Educational work with industrial management is also needed to make it realize that visual defects undoubtedly account for a considerable proportion of accidents and that "carelessness," to which 50 per cent of the accidents are attributed, is also partly the result of undiscovered visual defects among the industrial workers. There is needed a program of special training for such work which would provide for departments of industrial ophthalmology in all graduate schools of ophthalmology and for the development of a standard technic of examination and standard organization of ophthalmic care in industry.

DR. H. S. KUHN, Hammond, Ind.: It is not necessary to start with exact determinations. Ophthalmologists can greatly assist in placement if they do such simple things as eliminate all persons who lack depth perception from the lists of prospective crane operators, power machinists, tractor drivers and the like.

Distribution of Epidemic Keratoconjunctivitis in the United States. A. J. BEDELL, M.D., Albany, N. Y., J. A. M. A. **123:** 1101 (Dec. 25) 1943.

Keratoconjunctivitis is not a new disease. A number of severe and extensive outbreaks have

been reported in the literature. No race is exempt, and no particular occupation either predisposes to or is responsible for it.

The particular phase of this subject which the article discusses is the distribution of epidemic keratoconjunctivitis in the United States. A map is included which shows the location of the major outbreaks and the cities from which reports to the author were received for 1941 and 1942. An inspection of the map shows that in continental United States there have been four large outbreaks: In Portland, Ore., Rieke saw several hundred cases; in Seattle, Dawson reported hundreds of cases; in the San Francisco Bay area Nutting, Cordes, Hogan and Crawford and others treated several thousand patients, and in Schenectady, in the capital district of Albany, N. Y., thousands of persons had the disease.

The author gives the following summary and conclusions: A worldwide disease of the conjunctiva and cornea assumed epidemic proportions on the Pacific Coast and later in an inland city. The explanation of its predilection for some coastal cities in the West and its practically complete absence in similar localities in the East is something to engage the attention of the student.

Its failure to appear in any of the great army mobilization centers speaks well for the health of the men in service, as well as for the high standard of sanitation in the camps.

Keratoconjunctivitis is not a new disease. It affects young and old.

There has been no epidemic in the shipyards on the Gulf of Mexico or along the Atlantic Coast, a fact proving conclusively that it is not strictly a shipyard disease.

Because of the rush of war and the overwhelming number of cases it is possible that several diseases have been included under the term epidemic keratoconjunctivitis. It is certain that more complications and greater and more extensive ocular involvements were reported from the West Coast and Hawaii than were experienced in other parts of the country.

To infer that the epidemic spread throughout the United States is not warranted by the collected facts.

DISCUSSION

Dr. Thomas D. Allen, Chicago: This disease is not new to the world, but in the form in which it exists in the United States today it is new to ophthalmologists. The character of the disease seems to have changed, as in the Hammond, Ind., region Kuhn reported that keratitis now develops in only 10 per cent as compared with about 65 to 80 per cent at first. Any ophthalmologist who has had the disease, as I have, and has traced it to its source, as I did, would agree that it is contagious. In communities where it has suddenly gained access its control has been in direct proportion to the vigilance of the medical profession and the local boards of health. Soap and water constitute the first line of defense.

Dr. Michael J. Hogan, San Francisco: The results of Dr. Bedell's survey lead one to draw several conclusions: First, the epidemic on the Pacific Coast must have been initiated by patients who acquired the disease in the Hawaiian epidemic and carried the infectious agent to the mainland. Second, the disease first gained a foothold among ship workers and was spread rapidly among them both by close contact and by the considerable shifts in personnel which occurred during 1940 and 1941. One finds it difficult to explain the high incidence of the disease in industrial plants while the incidence in general population is relatively low. However, because of this the California State Industrial Accident Commission has ruled that the disease is compensable. The California State Superior Court has concurred in this finding. Many ophthalmologists have disagreed with this opinion.

Dr. A. J. Bedell, Albany, N. Y.: There is no justification for use of the term epidemic keratoconjunctivitis unless the cornea is involved. I approve of Dr. Hogan's disagreement with the California State Superior Court in concurring with the decision of the California State Industrial Accident Commission that the disease is compensable, "simply because the incidence of the disease was higher among shipyard workers than in the rest of the population."

Fever Therapy in Ophthalmology. F. C. Cordes, M.D., San Francisco, J. A. M. A. **124:** 14 (Jan. 1) 1944.

Injections of milk are of particular value in the treatment of infants, especially those with ophthalmia neonatorum, since the injections usually cause fever with a temperature of 100 to 103 F. This applies even though the sulfonamide compounds are used, as it has been shown that their action is greater in the presence of elevated temperatures.

Diphtheria antitoxin has many disadvantages, but its use in the treatment of sympathetic ophthalmia seems justified.

Typhoid vaccine is the most useful and generally employed agent to produce fever for the treatment of acute lesions of the eye and its adnexa. On the theory that vasodilation may

be a factor in the beneficial results, smaller doses administered over a longer period seem as effective and cause less shock and discomfort. The temperature reaction in a series of cases in which smaller doses were used corresponded closely to that obtained in a series in which the average first dose was 53,000,000 and the average second dose 80,000,000 organisms. There are certain rather definite contraindications to its use.

When a milder temperature response is indicated or the patient's condition does not warrant the use of typhoid vaccine, the employment of Coley's mixed toxins is advisable. This preparation is a mixture of toxins derived from killed cultures of Staphylococcus erysipelatis and Bacillus prodigiosus, which are grown separately, then mixed and finally diluted to a definite strength. It has the advantage that hospitalization is not necessary.

Omnadin, which consists of a mixture of protein substances obtained from nonpathogenic bacteria, various animal fats and lipids derived from bile, has a place in the treatment of acute conditions when shock therapy must be avoided but leukocytosis and a rise in the antibody content of the blood are desirable. It is not as effective as typhoid vaccine or other forms of foreign protein but can be used when they are contraindicated.

The use of malaria is not justified in treatment of ophthalmic diseases.

Hyperpyrexia induced by high frequency methods is still in the experimental stage. Further observations are necessary to disclose the conditions in which it is most effective and to establish the dosage compatible with safety.

Of the various physical means used to produce hyperpyrexia, air-conditioned cabinets of the Kettering hypertherm type are best. Production of fever by physical means is most efficacious in the treatment of gonorrheal conjunctivitis and syphilitic keratitis and iridocyclitis. It is particularly useful in the treatment of syphilitic diseases of the eye. Because of the severity of the treatment, it should be used only in cases in which other forms of therapy are unsatisfactory.

DISCUSSION

Dr. E. L. Goar, Houston, Texas: In recent years I have confined my efforts in fever therapy to the intravenous use of typhoid H antigen. This agent is preferred because it produces the same therapeutic results as the mixed vaccine, with less discomfort. This is the best treatment for anterior uveitis which is not of tuberculous or syphilitic origin. It is much less efficacious with posterior uveitis and is of doubtful value with optic neuritis.

Dr. S. R. Gifford, Chicago: In cases of acute iridocyclitis in the absence of syphilis the evidence of a bacterial agent is often wanting, while an exact bacteriologic diagnosis is usually impossible. Foreign protein therapy, with or without the sulfonamide compounds, is of considerable value. Typhoid vaccine administered by vein in the dosage recommended by Allen, 30,000,000 to 80,000,000 organisms, usually produces the desired effect. In cases of optic neuritis and retrobulbar neuritis large doses of thiamine hydrochloride are added. Hyperpyrexia by physical means has a definite place in the treatment of those forms of syphilis which are resistant to chemotherapy alone.

Dr. Grady Clay, Atlanta, Ga.: In the clinic, boiled milk is used, with good results. In private practice, I employ subcutaneous injections of a milk preparation and intravenous injections of typhoid vaccine. In every case in which intraocular operation is performed intramuscular injections of a foreign protein are given. They are used in all cases of bacteria-infected corneal ulcer, in all cases of intraocular inflammation and for severe types of optic neuritis, especially when associated with encephalitis.

Dr. F. C. Cordes, San Francisco: I agree with Dr. Gifford that sulfonamide compounds are so effective in treatment of ophthalmia neonatorum that milk injections are probably unnecessary. I agree with Clay that typhoid vaccine should not be given in the office or at home because of the possible reactions that may at times be encountered in its use.

Chemotherapy in Ophthalmology. P. Heath, M.D., Detroit, J. A. M. A. **124:** 152 (Jan. 15) 1944.

When several agents are equally effective in meeting a problem, low toxicity and freedom from sensitization reactions or late harmful effects should govern the selection. The effective dose and concentration vary with different infections and different patients. In treatment of inclusion blennorrhea, sulfathiazole was used internally and locally. Gonorrheal ophthalmia or conjunctivitis are effectively treated with oral doses of sulfapyridine, sulfathiazole or sulfanilamide, ice compresses for any considerable edema (occasionally canthotomy), antiseptic irrigations and an ointment containing a sulfonamide compound. Therapy of hemolytic staphylococcus conjunctivitis consists of the administration of staphylococcus toxoid and local application of

antiseptic lotions and a sulfonamide ointment. For pneumococcic conjunctivitis (except that due to the Friedländer type) tyrothricin is used. In treatment of pneumokeratitis the oral administration of a sulfonamide compound is added. In the management of severe traumatic injuries general chemotherapy is necessary. In cases of epidemic keratoconjunctivitis the most favorable results have been obtained with tyrothricin. In cases of keratitis and ulcer due to Bacillus pyocyaneus, early treatment with sulfapyridine or sulfadiazine is indicated. Treatment of dendritic keratitis by local application of tyrothricin, with repeated pasteurization by cautery, has led to the most rapid cure. Blepharitis and the form of punctate keratitis associated with chronic conjunctivitis are sometimes cured by use of sulfonamide ointments; tyrothricin and the disease compound neo-synephrine sulfathiazolate has relieved some obstinate forms of the disease. In treatment of orbital abscess one of the sulfonamide compounds, hot compresses and drainage are employed. With thrombosis of the cavernous sinus a high dosage of sulfadiazine is used. In cases of uveitis the causative agent is attacked. Sulfonamide compounds may be of value. In treatment of trachoma sulfanilamide is the drug of choice. The drug reduces secondary infections and causes improvement in corneal involvement. The progress of postoperative infection may be checked by the use of sulfadiazine or sulfapyridine. With low grade dacryocystitis irrigation with a solution of tyrothricin through the lacrimal sac is indicated.

DISCUSSION

Dr. Alan C. Woods, Baltimore: I am in general agreement with Dr. Heath as to the value of the sulfonamide compounds, but my results with tyrothricin have not been so happy. In treatment of recurrent iritis, tuberculous uveitis, choroiditis and sympathetic ophthalmia, the use of sulfonamide compounds has repeatedly been without favorable therapeutic effects. The present indication is that penicillin will probably be the most effective agent against infection with the gram-positive organism.

Dr. W. S. Atkinson, Watertown, N. Y.: The nonspecific use of sulfonamide compounds should be avoided, and their local use in postoperative medication is contraindicated.

Dr. J. G. Bellows, Chicago: The sulfonamide compounds must be used with caution in treatment of traumatic lesions of the cornea because in the absence of normal epithelium they cause severe injury. In the treatment of epidemic keratoconjunctivitis "sulfathiazole desoxyephedrine" reduces rapidly the subjective symptoms and the redness and swelling, without influencing the scarring.

Dr. R. C. Gamble, Chicago: In cases of sympathetic ophthalmia the sulfonamide compounds hold the progress of the disease in check, giving time for the natural healing processes of the ocular tissue to act.

Industrial and Domestic Injuries of the Eye. C. P. Clark, M.D., Indianapolis, J. A. M. A. **124:** 157 (Jan. 15) 1944.

The author gives the following summary:

The prevention of ocular injuries commands an important place in industry, agriculture and the home.

Efficient first aid treatment is important in reducing the loss of man hours of work, in relieving the suffering associated with the injury and, most important of all, in retaining useful vision of the injured eye.

Penetrating and nonpenetrating wounds are treated according to the rules which years of experience of members of the medical profession have proved best.

Particular care should be taken to avoid sympathetic ophthalmia when there has been an injury of the uveal tract, especially of the ciliary body.

DISCUSSION

Dr. W. F. Holzer, Worcester, Mass.: In my community most injuries are foreign bodies in the cornea or abrasions of the cornea. My practice is to remove the foreign body, curet the cornea thoroughly, cauterize with 95 per cent phenol and leave the eye uncovered. Sulfathiazole (5 per cent ointment) is applied to the lower cul-de-sac, and a tube of ointment containing 1 per cent phenacaine hydrochloride and epinephrine (1:50,000) is dispensed, to be used every hour or two as required.

Dr. H. L. Blair, Rochester, Minn.: A common error is the failure to remove early enough of the blood clot that fills the anterior chamber after contusion. Many such eyes have been lost, owing to hematogenous infiltration of the cornea and secondary glaucoma. There is overuse of the conjunctival flap for penetrating laceration of the cornea. The larger corneal lacerations should be closed with corneal sutures ¼ inch (0.6 cm.) apart.

Dr. E. W. Griffey, Houston, Texas: A simple and effective remedy for flash burns of the eye after exposure to the welder's arc, which in

the initial phase amounts to good prophylaxis, is the use of three successive instillations of 1:1,000 solution of epinephrine hydrochloride at five minute intervals shortly after onset of ocular pain following flash burn, and before objective signs are too obvious.

DR. ALBERT C. SNELL, Rochester, N. Y.: In industry, adequate provisions for rendering such aid should be available in every plant, both large and small. These provisions should include proper equipment and supplies, as well as definite written instructions to be followed by the available personnel. In my opinion, small or medium-sized prolapsed parts of the ciliary body should be amputated thoroughly, but one should always be alert to the possibility of sympathetic involvement. In minor degrees of prolapse of the choroid, usually with some vitreous, amputation should be done and prophylactic treatment employed.

DR. C. P. CLARK, Indianapolis: The subject can be summarized briefly: an aggressive educational campaign to prevent accidents where they are most likely to occur; prompt and efficient emergency care for the injured, and employment of good ophthalmic surgical practice for persons more seriously injured. The methods for accomplishing these aims may vary according to the locality and the facilities that are available.

1930 Chestnut Street.

Book Reviews

Manual of Diseases of the Eye. By Charles H. May, with the assistance of Charles A. Perera. Eighteenth Edition. Price, $4. Pp. 520, with 387 illustrations, including 32 plates and 93 colored figures. Baltimore: William Wood & Company, 1943.

The present edition, appearing three years after the preceding one, has been revised and brought up to date. The chapters "Lacrimal Apparatus" and "Errors of Refraction" have been rewritten. The latter has been contributed by Dr. Alson E. Braley, assistant professor of ophthalmology, Columbia University College of Physicians and Surgeons.

Among the changes made in this revision, mention should be made of the following two: compensation for ocular eye injuries and the requirements for admission to the military services of the Army of the United States.

The book remains in this revised edition a most reliable manual of instruction for the student and the general practitioner.

ARNOLD KNAPP.

Studies from the School of Medicine, the George Washington University for 1942-1943. Washington, D. C., 1943.

Under this title, 43 reprints have been bound together to represent the literary output for 1942 and 1943. A great variety of subjects are included, and the various departments of the university are ably represented. From the department of ophthalmology the director, Dr. W. T. Davis, has contributed the following two articles: "Differential Diagnosis of Paresis of the Oblique and the Superior and Inferior Recti Muscles" (*Tr. Am. Acad. Ophth.* **47**:206, 1943) and "Differential Diagnosis of the Tropias, with Special Reference to the Value of Orthoptic Training" (*Am. J. Ophth.* **25**:697, 1942).

ARNOLD KNAPP.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Comparative Ophthalmology

CHOLINE ESTERASE AT THE NERVE TERMINATION IN THE SPHINCTER PUPILLAE OF THE TURTLE. P. B. ARMSTRONG, J. Cell. & Comp. Physiol. **22:** 1 (Aug.) 1943.

Experiments on preparations of the iris of the young Cumberland tortoise (Pseudemys elegans), which possess a striated sphincter pupillae, led to results which differed distinctly from those which the author reported for amphibian eyes. The responses of this muscle to stimulation with acetylcholine, physostigmine, nicotine, atropine and the electric current through the afferent nerve fibers were similar to those of the superior cervical ganglion of the cat, reported by Feldberk and Vartiainen, and to those of the striated sphincter iridis of the bird, reported by Dale. They showed high thresholds for acetylcholine and marked potentiation by physostigmine. High concentrations of atropine were necessary to reduce the response to acetylcholine. The initial stimulation of the sphincter with nicotine was followed by paralysis. This group of responses of the sphincter iridis of the tortoise characterizes the "nicotine" action of acetylcholine, whereas the "muscarine" effects are evident in the amphibian sphincter pupillae. In contrast to the latter, high concentrations of choline esterase appeared to be present in the afferent nerve terminations of the sphincter pupillae of the tortoise. L. VON SALLMANN.

General Diseases

TEMPORAL ARTERITIS. L. T. POST and T. E. SANDERS, Am. J. Ophth. **27**:19 (Jan.) 1944.

Post and Sanders report the case of a housewife aged 66 who came under observation because of failing memory and mental deterioration. The left temporal artery was prominent, thickened and tortuous and the surrounding tissue hyperemic. A section of the right temporal artery, which showed similar changes, was removed for examination, and definite changes were noted. The retinal arteries showed pronounced sclerosis, with irregularity of caliber and thickening of the walls, and in places sheathing. The patient died suddenly of a cerebral hemorrhage. The authors discuss temporal arteritis. They believe that no particular ocular lesion is characteristic.

W. S. REESE.

Glaucoma

NEVUS FLAMMEUS ASSOCIATED WITH GLAUCOMA: REPORT OF A CASE IN WHICH CYCLODIATHERMY WAS USED IN AN ATTEMPT TO CONTROL THE INTRAOCULAR PRESSURE. B. Y. ALVIS and V. A. TOLAND, Am. J. Ophth. **26:** 720 (July) 1943.

A boy aged 14 years had a naevus flammeus on the right side of the face which conformed in outline with the cutaneous distribution of the ophthalmic and maxillary branches of the right trigeminal nerve. The nevus was also present on the mucous membranes of the nose and throat and followed the same distribution. The right eye showed hydrophthalmos, with a tension of 43 mm. of mercury (Schiøtz). There was deep, glaucomatous cupping of the optic nerve. A corneoscleral trephine was done, but the opening closed. Vogt's cyclodiathermy was then carried out. About six months later the tension was 16.5 mm. of mercury, and corrected vision was 5/75. A Bjerrum scotoma was present in the field of vision.

W. ZENTMAYER.

Hygiene, Sociology, Education and History

ASPECTS OF BRAZILIAN OPHTHALMOLOGY. M. E. ALVARO, Am. J. Ophth. **26:** 474 (May) 1943.

Alvaro traces the progress of ophthalmology in Brazil and describes the present day management of certain diseases of the eye that are encountered in that country. A board of ophthalmology is now operating in Brazil.

W. ZENTMAYER.

REHABILITATION OF THE UNI-OCULAR PATIENT. C. G. SCHURR, Brit. J. Ophth. **27:** 467 (Oct.) 1943.

It is desirable that active steps to reeducate the disabled be taken as soon as possible and such reeducation may commence within a day or two of the removal of the eye.

Schurr gives an account of the methods employed in cooperation with the rehabilitation department of the Royal Sussex County Hospital. The treatment is both physiologic and psychologic.

W. ZENTMAYER.

Injuries

A Case of Removal of Non-Magnetic Foreign Body from the Ciliary Region. D. Pierse, Brit. J. Ophth. **27:** 550 (Dec.) 1943.

Following the technic of Spaeth, Pierse removed a piece of brass from the ciliary region. An attempt was first made to remove the foreign body through a corneal incision; as a result, it disappeared backward through the hole in the iris. A needle was inserted at the estimated position of the foreign body, and its exact location was determined by a roentgenogram. A trap door opening, with the hinge of the flap at the limbus, was made in the sclera, and the foreign body was easily removed through the ciliary body. Pierse comments that had a roentgenogram been taken immediately the attempted removal through the cornea would have been averted.

The article is illustrated. W. Zentmayer.

Methods of Examination

Further Observations on Autofundoscopy (Auto-Ophthalmoscopy of Eber; Purkinje Figure of Walker). L. C. Drews, Am. J. Ophth. **26:** 1143 (Nov.) 1943.

Drews draws the following conclusions:

"1. Widening of the afterimage of the filaments, as seen with my slightly myopic eye, is due chiefly to chromatic aberration.

"2. An apparatus for measuring muscle balance or for determining the presence of normal retinal correspondence can be made by simply mounting a strong plus cylinder on a paper tube of a length equal to the focal length of the cylinder and stretching a heavy rubber band across the cylinder between the axis marks. With a second tube, similarly prepared, it is possible to study binocular afterimages simultaneously produced.

"3. The decrease in size of the optic disc as seen by autofundoscopy probably is due to the 'filling up of the blind spot.'

"4. Scotomas in the central 10 degrees of the field do not show any appreciable tendency toward 'filling up,' as is evidenced by accurate measurement of these scotomas by autofundoscopy.

"5. Autofundoscopy requiring flooding of the eye with light may make it possible to visualize a paracentral area of the retina where retinal function is normal, except that regeneration of visual substance is delayed (case 5). This is wholly hypothetic.

"6. If a scotoma in the central 10 degrees of the field did show 'filling up' comparable to the filling of the scotoma of the optic nerve, it would be seen with autofundoscopy to be much smaller than it really is. Do congenital scotomas due, for instance, to coloboma of the choroid, show this?"

W. S. Reese.

Neurology

Changes in the Eyes in Amaurotic Family Idiocy (Infantile Type of Tay-Sachs Disease): Histopathologic Observations in a Case. G. Hassin, Arch. Neurol. & Psychiat. **49:** 628 (April) 1943.

"The eyes, together with the brain and spinal cord, in a typical case of amaurotic family idiocy, were removed sixteen hours after death.

"The following conclusions are drawn from the study of this material:

"1. The changes in the retina and optic nerves in patients suffering from amaurotic family idiocy are analogous to the changes in the central nervous system in general.

"2. The perioptic spaces exhibit the presence of elements similar to those seen in the subarachnoid spaces of the brain and spinal cord.

"3. The hyperplasia of the pial septums in the optic nerves is analogous to that of the piaarachnoid and is a reaction of the latter to the presence of abnormal products of activity of the ganglion cells discharged there by way of the perioptic spaces.

"4. Status spongiosus—a manifestation of severe destruction of nerve tissue—is a striking feature in the changes in the optic nerve associated with amaurotic family idiocy."

R. Irvine.

Integrated Facial Patterns Elicited by Stimulation of the Brain Stem. E. Weinstein and M. Bender, Arch. Neurol. & Psychiat. **50:** 34 (July) 1943.

"The facial patterns as they occur normally in the monkey and in man are both voluntary and involuntary. They resemble automatic, stereotyped movements, such as walking or swimming, which to a considerable degree are performed unconsciously. The question is where these facial movements are integrated in the nervous system. According to Ranson, the subthalamus serves as a regulator and coordinator of such somatic functions. Direct stimulation of the subthalamus has indicated (Bard; Hinsey) that this structure is an integrating center for both the somatic and the visceral components of emotional expression, efferent paths making connections with the primary motor nuclei of the brain stem and the spinal cord. However, in our experiments stimulation of the monkey's hypothalamus failed to produce any coordinated facial expressions unless currents stronger than those previously described were used. Furthermore, there is no reason to believe that our responses from the brain stem were elicited from descending hypothalamic pathways. On the basis of our experiments, it seems that the brain stem is an important integrator of somatic functions of the cranial muscles.

"Stimulation of designated areas in the tegmentum of the brain stem of the macaque monkey with the Horsley-Clarke stereotaxic technic produces facial patterns integrated with other somatic and automatic components into purposeful acts.

"The facio-ocular synkinesis of contraction of the orbicularis oculi muscles, upward rolling of the eyeballs and constriction of the pupils can be elicited from the reticular substance of the pons 1.5 to 2.5 mm. lateral to the midsagittal plane.

"Contraction of the orbicularis oris muscle in a sucking, swallowing movement is associated with elevation of the base of the tongue, raising of the uvula and inhibition of respiration in the inspiratory phase. This pattern is elicited from the reticular formation of the medulla 0.5 to 1.5 mm. from the midsagittal plane dorsomedial to the rostral part of the inferior olive.

"A faciorespiratory complex simulating laughter and consisting of retraction and elevation of the corners of the mouth, depression of the lower jaw, lowering of the base of the tongue and uvula and cessation of respiration in the expiratory phase can be elicited from an area 0.5 to 2 mm. from the midsagittal plane dorsomesial to the inferior olive.

"It is suggested that the facio-ocular and facio-respiratory synkinesias are integrated in the reticular formation of the brain stem."

R. IRVINE.

TUBEROUS SCLEROSIS. A. Ross and W. DICKERSON, Arch. Neurol. & Psychiat. **50:** 233 (Sept.) 1943.

This unusual disease is congenital and may be hereditary or familial. The clinical material on which this paper is based was derived from the study of 25 patients. The basic characteristics of tuberous sclerosis are developmental anomalies in tissues of ectodermal origin, particularly the brain, skin and retina; defective development and tumor formation are not infrequently manifested elsewhere.

The usual clinical criteria for the recognition of tuberous sclerosis are adenoma sebaceum on the face, retinal tumors, mental deficiency and convulsions, although it is not necessary for all these qualifications to be fulfilled in order that the diagnosis be established. At times sebaceous adenoma is the only sign of the disorder. The retinal lesions, as a rule, consist of whitish gray nodules (phakomas), which may be single or multiple, flat or raised, may be situated anywhere on the fundus and ordinarily are not directly connected with blood vessels.

Six patients in the series had retinal tumor, in 1 of whom the lesion was bilateral. In 4 patients the tumor appeared either to have its origin at the margin of the disk or to cover the major portion of the disk itself. In the 2 remaining patients the involved area was situated above and temporal to the disk.

An autopsy in 1 case with involvement of the eye is reported in detail. The retinal nodules were areas of gliosis composed of cells of a type not entirely clear, but probably astrocytic or astroblastic. This adds support to the theory of the glial origin of the tumor.

R. IRVINE.

STUDIES IN DISEASES OF MUSCLE: XIV. PROGRESSIVE MUSCULAR ATROPHY OF PERONEAL TYPE ASSOCIATED WITH ATROPHY OF THE OPTIC NERVES; REPORT ON A FAMILY. A. MILHORAT, Arch. Neurol. & Psychiat. **50:** 279 (Sept.) 1943.

The occurrence of progressive peroneal muscular atrophy associated with progressive bilateral optic nerve atrophy in 2 brothers is described. Cases of a similar disease in 8 members of 6 families were reported previously, with 2 other members having typical muscular changes but no visual disturbance. All the patients were males; the occurrence of the syndrome in females appears not to have been observed. A sister of the 2 patients described in this report had bilateral optic nerve atrophy and a disease which most probably was disseminated sclerosis. The relation, if any, between the condition in the brothers and that in the sister is at present not understood. It appears likely that the syndrome described in this report represents either a clinical entity which is different from the muscular conditions usually recognized or a definite form of progressive peroneal muscular atrophy.

R. IRVINE.

Ocular Muscles

THE PARENTS' ROLE IN ORTHOPTIC TRAINING. F. WALRAVEN, Am. J. Ophth. **26:** 1175 (Nov.) 1943.

Walraven gives the following summary:

"The parents should understand fully the following points:

"1. Sufficient knowledge of binocular vision is essential.

"2. The time necessary for the developing of binocular vision varies with the individual.

"3. In selected cases of amblyopia, occlusion is always necessary.

"4. The child's response to occlusion largely depends on the attitude of the parents.

"5. Home exercises must be thoroughly understood before they are practiced.

"6. Stimulation is necessary for the required mental effort.

"7. Surgery cannot accomplish alone what it does in conjunction with orthoptic training.

"8. Full cooperation with ophthalmologist and technician is necessary to a successful training period."

W. S. REESE.

A METHOD OF EVALUATION OF BINOCULAR MUSCLE BALANCE. D. D. S. STEWART, Brit. J. Ophth. **27:** 477 (Nov.) 1943.

Stewart describes a rapid method of estimating, as a part of the routine ophthalmic examination, the dynamic ocular equilibrium for distance. He believes that daily familiarity with the variability of functions concerned with binocular muscle balance and their association with visual comfort will reconcile prevalent exaggerated skepticism and enthusiasm about the whole subject.

The article is illustrated. W. ZENTMAYER.

Operations

IMPROVED TECHNIQUE FOR IMPLANTATION OF A BALL IN TENON'S CAPSULE. F. H. VERHOEFF, Am. J. Ophth. **26:** 1057 (Oct.) 1943.

The conjunctiva is incised close to the limbus and then, with all the underlying tissue down to the sclera, is carefully dissected from the globe; at this stage the conjunctiva is not dissected from Tenon's capsule. After removal of the eye, the glass ball is inserted and pushed back in the orbit. Tenon's capsule is grasped near the cut end of the tendon of the external rectus muscle, and a tongue, consisting of two layers of the capsule, is pulled forward. About 5 mm. behind the end of the tongue two needles of a double-armed catgut suture are passed through the tongue from beneath, the vertical distance between them being about 6 mm. The two needles are then passed from beneath through a similar tongue in front of the tendon of the internal rectus muscle. Then they are passed from beneath a tongue in front of the superior rectus muscle, one in front of the other, the upper being about 7 mm. behind the end of the tongue and the lower about 3 mm. farther back. The needles are then passed through a tongue in front of the tendon of the inferior rectus muscle, the lower needle being the one farther back. The ends of the sutures are then pulled on until all four tongues are brought together in front of the ball. The suture is then tied securely and cut close to the knot. The conjunctival opening is closed horizontally by a continuous silk suture. At the completion of the operation a form is placed in the conjunctival sac.

W. ZENTMAYER.

Physiology

FUSION, PROJECTION, and STEREOPSIS. I. FRANKLIN, Am. J. Ophth. **25:** 1316 (Nov.) 1942.

Stereopsis, fusion and projection are not purely sensory or sensory-psychic abstractions, but are eye-limb-body, locomotion and prehension functions, in which the body and limb movements have evolved from an actual to a potential form.

W. S. REESE.

CLINICAL VASCULAR PHYSIOLOGY OF THE EYE. W. F. DUGGAN, Am. J. Ophth. **26:** 354 (April) 1943.

Duggan discusses a number of retinal and other lesions, the results of homeostatic reactions which are physiologic in nature but pathologic in degree. Many of these lesions have been attributed to toxins, foci of infection and allergy. All can be interpreted as due to variations in the arterioles and capillaries which differ quantitatively from the normal. The cause is usually endogenous.

W. ZENTMAYER.

Refraction and Accommodation

HIGH CONGENITAL MYOPIA WITH CONVERGENT STRABISMUS. R. C. GAMBLE, Am. J. Ophth. **27:** 159 (Feb.) 1944.

Gamble draws the following conclusions:

"1. High congenital myopia and convergent strabismus are often associated.

"2. The myopia is lenticular in origin and relatively nonprogressive, at least up to the age of adolescence.

"3. The convergent strabismus is of low degree, is usually corrected by glasses, and is, on the whole, relatively unimportant."

W. S. REESE.

A NEW APPROACH TO CROSS CYLINDER TESTS. J. I. PASCAL, New York State J. Med. **43:** 323 (Feb. 15) 1943.

This article discusses the chief difficulty in application of cross cylinder tests, which is the fact that the patient often has to compare images made up of diffusion spots of different shapes, as well as of different sizes. Thus, he frequently has to say that the letters in the two positions of the cross cylinder are blurred about equally, but in a different way. The article explains the reasons for this behavior and develops a method of using cross cylinders so that this difficulty is eliminated.

It is possible to apply cross cylinders for testing and correcting astigmatism in the same way as spherical lenses are used for testing and correcting hyperopia and myopia. The same charts can be used, and, what is especially significant, the changes produced in the patient's retinal images are the same as those produced during a test for a spherical error. The procedure is to change the astigmatism to equally mixed astigmatism and maintain it thus throughout the test by the use of correcting cross cylinders. In this way, the patient will have to compare images made up of diffusion circles of different sizes, exactly as he does during a test with spherical lenses for a spherical error.

W. ZENTMAYER and J. I. PASCAL.

Uvea

ENDOPHTHALMITIS DUE TO B. SUBTILIS FOLLOWING INJURY. A. B. REESE and D. KHORAZO, Am. J. Ophth. **26:** 1251 (Dec.) 1943.

Reese and Khorazo report the case of a man aged 56 in whom acute iridocyclitis with hypopyon followed an injury from an intraocular foreign body. The eye was enucleated. Bacillus subtilis was present which was not pathogenic for guinea pigs but induced endophthalmitis when injected into the anterior chamber of a rabbit's eye.

W. S. REESE.

IRIDO-CYCLITIS AND CHOROIDITIS DUE TO "SILENT" SINUSITIS. R. FORD, Brit. J. Ophth. **27:** 469 (Oct.) 1943.

The author cites the histories of 2 patients to show how elusive, even with every advantage for expert diagnosis, the cause of uveitis may be; she also gives the histories of 3 other patients to demonstrate that elimination of a focus of infection in the sinuses, even when there is no evidence of its existence other than the uveitis, may lead to prompt and permanent cure. She concludes that if all investigations prove negative in a case of uveitis, latent sinusitis should be suspected and treated.

W. ZENTMAYER.

VOGT-KOYANAGI SYNDROME. L. J. MONTALVO DURAND, Bol. Asoc. Méd. de Puerto Rico. **35:** 218 (June) 1943.

According to Montalvo Durand, the Vogt-Koyanagi syndrome is rare. The most important symptoms are nontraumatic bilateral uveitis; premature graying; alopecia; symmetric vitiligo, especially on the hands, wrists and feet, and dysacousia. The cause is unknown. Japan is the place of greatest incidence. The disease develops most frequently in persons between 30 and 40 years of age. Syphilis and tuberculosis have a certain contributory significance in the development of the disease.

J. A. M. A. (W. ZENTMAYER)

Therapeutics

INTRAOCULAR INJECTION OF SULFANILAMIDE IN A CASE OF PURULENT IRIDOCYCLITIS. J. IGERSHEIMER, Am. J. Ophth. **26:** 1045 (Oct.) 1943.

In a case of purulent iridocyclitis traumatica enucleation was planned because of great irritation and absence of sensitivity to light. After injection of sulfanilamide into the anterior chamber inflammation disappeared, and final vision was 20/40.

W. ZENTMAYER.

X-RAY THERAPY OF INFLAMMATORY AND NEOPLASTIC DISEASES OF THE EYE. J. BORAK, Am. J. Ophth. **26:** 1170 (Nov.) 1943.

Borak refers briefly to the radiosensitivity of the different tissues of the eye and to lesions amenable to roentgen ray therapy, giving a list of these lesions and the effect of treatment.

W. S. REESE.

News and Notes

GENERAL NEWS

Postponement of Second Pan-American Congress of Ophthalmology.—The second Pan-American Congress of Ophthalmology, which was scheduled to be held in November 1944 in Montevideo, Uruguay, has been postponed until the fall of 1945, particularly because of transportation difficulties.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

Presdient: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Dr. A. MacRae, 6 Jesmond Rd., Newcastle-upon-Tyne, England.
Secretary: Dr. Percival J. Hay, 350 Glossop Rd., Sheffield 10, England.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Secretary: Mr. L. H. Savin, 7 Queen St., London, W. 1, England.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.
Place: Oxford, England. Time: July 8-9, 1943.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

Polish Ophthalmological Society

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Dr. W. Belfort Mattos, Caixa Postal, 4086, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 III tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York City.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
Place: Chicago. Time: June 12-16, 1944.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Lawrence T. Post, Metropolitan Bldg., St. Louis.
President-Elect: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
Executive Secretary-Treasurer: Dr. William L. Benedict, 101–1st Ave. Bldg., Rochester, Minn.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. John Green, 3720 Washington Ave., St. Louis.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.
Place: Halifax, N. S. Time: Aug. 4-5, 1944.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. L. L. Bull, 1215–14th Ave., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

Rock River Valley Eye, Ear, Nose and Throat Society

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. M. H. Pike, Midland, Mich.
Secretary-Treasurer: Dr. R. H. Criswell, 407 Phoenix Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July and August.

Sioux Valley Eye and Ear Academy

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

Southwestern Academy of Eye, Ear, Nose and Throat

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

Southwestern Michigan Triological Society

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

Western Pennsylvania Eye, Ear, Nose and Throat Society

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

Arkansas State Medical Society, Eye, Ear, Nose and Throat Section

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

Colorado Ophthalmological Society

President: Dr. C. A. Ringle, 912–9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

Eye, Ear, Nose and Throat Club of Georgia

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings, Mont.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr B. E. Failing, 31 Lincoln Park, Newark.
Secretary: Dr. George Meyer, 410 Haddon Ave., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. James E. McAskill, 508 Woolworth Bldg., Watertown.
Secretary: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

West Virginia State Medical Association, Eye, Ear, Nose and Throat Section

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.
Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

Akron Academy of Ophthalmology and Otolaryngology

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.
Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.
Time: First Monday in January, March, May and November.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.
Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.
Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

Birmingham Eye, Ear, Nose and Throat Club

President: Each member, in alphabetical order.
Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.
Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

Brooklyn Ophthalmological Society

President: Dr. William B. Agan, 1 Nevins St., Brooklyn.
Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.
Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.
Time: Second Thursday of each month.

Chattanooga Society of Ophthalmology and Otolaryngology

President: Each member, in alphabetical order.
Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.
Place: Mountain City Club. Time: Second Thursday of each month from September to May.

Chicago Ophthalmological Society

President: Dr. Vernon M. Leech, 55 E. Washington St., Chicago.
Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago.
Place: Chicago Towers Club, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

Cincinnati General Hospital Ophthalmology Staff

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.
Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.
Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

Cleveland Ophthalmological Club

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.
Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.
Time: Second Tuesday in October, December, February and April.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.
Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. H. D. Emswiler, 370 E. Town St., Columbus, Ohio.
Secretary-Treasurer: Dr. D. G. Sanor, 206 E. State St., Columbus, Ohio.
Place: The Neil House. Time: 6 p. m., first Monday of each month.

Corpus Christi Eye, Ear, Nose and Throat Society

Chairman: Dr. Arthur Padillo, 414 Medical Professional Bldg., Corpus Christi, Texas.
Secretary: Dr. Edgar G. Mathis, 815 Medical Arts Bldg., Corpus Christi, Texas.
Time: Second Friday of each month from October to May.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. Abell Hardin, Medical Arts Bldg., Dallas, Texas.
Secretary: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.
Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.
Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit.
Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month, November through April.

Detroit Ophthalmological Society

President: Dr. Parker Heath, 1553 Woodward Ave., Detroit.
Secretary: Dr. Leland F. Carter, 1553 Woodward Ave., Detroit.
Place: Club rooms of Wayne County Medical Society. Time: Third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.
Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Eastern Pennsylvania Association of Eye, Ear, Nose and Throat Physicians

President: Dr. James E. Landis, 232 N. 6th St., Reading.
Secretary-Treasurer pro tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April each year.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.
Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-Laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. M. E. Trainor, 523 W. 6th St., Los Angeles.

Secretary-Treasurer: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time. 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Edwin C. Bach, 324 E. Wisconsin Ave., Milwaukee.

Secretary-Treasurer: Dr. Ralph T. Rank, 238 W. Wisconsin Ave., Milwaukee.

Place: University Club. Time: 6:30 p. m., second Tuesday of each month.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.

Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.

Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.

Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.

Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.

Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashvile, Tenn.

Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.

Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-Laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.

Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.

Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Frank C. Keil, 660 Madison Ave., New York.
Secretary: Dr. Willis S. Knighton, 121 E. 61st St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Milton Berliner, 57 W. 57th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: Squibb Hall, 745–5th Ave. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Wilfred E. Fry, 1819 Chestnut St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. John B. McMurray, 6 S. Main St., Washington, Pa.
Secretary: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. R. M. Brickbauer, Shillington, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from October to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.
Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. S. Bockoven, 1752 Massachusetts Ave., Washington, D. C.
Secretary-Treasurer: Dr. John Lloyd, 1218–16th St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.